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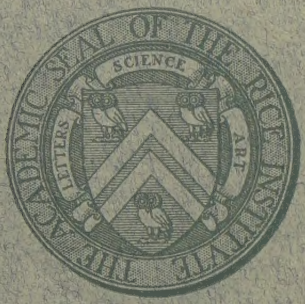

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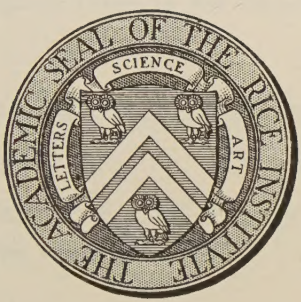

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VITAMINS IN HUMAN NUTRITION[1]

I

VITAMINS: THE SPARK PLUGS OF THE BODY

THE food of man, like his labors and pleasure, has undergone great changes during the half-million years or more since our ancestors fought out their struggle for existence with mammoths and cave bears instead of tax collectors and strike organizers. In the days of leopard-skin dinner jackets, when daylight-saving time and nudism were in their original heyday, man lived on a good variety of meat, fish, insects, shellfish, fruits, seeds, tubers, and sprouts —whatever he could knock down or pick up with the minimum of effort or thought. At the dawn of civilization and ever since, with all due respect to the orators who speak of the "right" to work, and extol work as a divine blessing, man, like every other animal on the earth, has endeavored to get his daily rations and other necessities and pleasures with the least possible expenditure of energy.

It was easier to herd sheep and goats than to chase antelopes through the jungle, and easier to collect the grain from concentrated fields of corn or rice than to roam for miles to collect enough herbs or roots to satisfy a gnawing stomach. Thus animal husbandry and agriculture developed and man's food became less varied. But it was not until even later days, when men found it easier to work in mills, or sail in ships, or write books, or even sit on flagpoles, than to hoe corn or

[1]A series of current popular lectures by Asa Crawford Chandler, Ph.D. (California), Professor of Biology at the Rice Institute.

herd sheep, that the diet became sufficiently restricted or sufficiently manipulated to make deficiencies develop to an appreciable extent.

Diseases now recognized as due to dietary deficiencies have lost their birth certificates, but they date back to at least 2600 years B.C., when a Chinese author wrote a description of beri-beri. Eye troubles and night blindness were described in ancient Chinese and Egyptian writings, and remedies prescribed for them. The Egyptians fed liver as a cure, but the Chinese put their faith in concoctions made from droppings of flying foxes and bats. Both prescriptions are rich in vitamin A, lack of which is now known to be the cause of these eye troubles. Ever since men have been going down to the sea in ships, scurvy has been a curse of the seafarer, and was variously attributed to exposure to cold, to sea air, to salted meats, or to annoyed deities.

"Spring fever," through the ages, has driven farmers to eat the first sorrel or dandelion greens that followed the melting snows to satisfy a craving for vitamin A, lack of which was very common during winter days before the era of canned and frozen vegetables banished the seasons as far as this vitamin is concerned.

In the case of nearly all fundamentally important scientific discoveries, a few accurate observers hit upon truths which become established facts only after years of labor and experiment, while a few clairvoyant thinkers actually hurdle decades or even centuries to make startlingly accurate predictions. So it has been with the discovery of vitamins. It was not, however, until the twentieth century was outgrowing diapers that the realization became general that man cannot live by bread alone, even nutritionally speaking. Even with a diet perfectly adequate in calories, with a good mixture of proteins containing all the necessary amino acids,

and with a good supply of pure carbohydrates, fats, and minerals, something more was needed not only to keep a body in good working order and free from disease, but even to allow it to grow at all.

The "discovery" of a vitamin is usually dated from its isolation in a fairly pure state, but recognition of a deficiency, and foods capable of supplying it, may long antedate such a discovery, and it may be years afterwards before the actual chemical composition is worked out. The cure of scurvy by feeding citrus juice or green vegetables was announced by Kramer over two hundred years ago, and a ration of lemon juice was made compulsory in the British navy while Washington was still President of the United States. Ever since then British sailors, who erroneously called their lemons "limes," have been nicknamed "limies." It was not, however, until two Norwegian scientists, Holst and Frölich, had spent several years, from 1907 to 1912, experimenting with guinea pigs that enough was known about the scurvy-preventing constituent of foods so that it could be admitted to the once exclusive family of accessory alphabetically-designated food factors, which Drummond named "vitamins" in 1920. The name "vitamine" had been coined by a Polish scientist, Casimir Funk, in 1911, for an approximately pure extract of rice polishings which would cure beri-beri. The term "amine," signifying in chemistry a certain type of nitrogenous compound, while applicable to vitamin B, is inappropriate for other vitamins. Drummond cleared his own conscience and soothed the outraged feelings of the chemists by amputating the final "e" and thus doing away with any chemical connotations the word might have. The final isolation and identification of the pure chemical substance which is vitamin C stripped bare required the combined work of Hungarian, British, German, and American workers from

1927 until 1932. Who, then, can be said to have discovered vitamin C? The situation is almost as complicated for the other vitamins.

The vitamins are a peculiar hodge-podge of substances as unrelated as the drugs on an apothecary's shelf. The drugs constitute a natural grouping not because of what they are, but because of what they do, and this is true of vitamins also. The drugs have only one thing in common—they restore health or alter body functions when taken in relatively small quantities; the vitamins also have one thing in common—they *maintain* health and normal body functions when taken in relatively *minute* quantities. The amazing physiological effects they can bring about in almost incredibly small doses, and the widespread disorders which follow upon their absence, together with, until the last decade, their unknown chemical nature, has given them an aura of mystery and romance which has appealed to the popular imagination, and made them subjects of popular consciousness to a degree to which other food essentials, such as amino acids or minerals, may never aspire. But, actually, there is no longer very much excuse for segregating vitamins into an exclusive fraternity. One writer recently expressed the belief (or hope) that the name "vitamin" will eventually join the musty company of "phlogistic humors," "animalcules," and kindred antiquated terms. The striking physiological effects of small doses is also true of minerals, and nearly all the vitamins so far known to exist have yielded up the hidden secrets of their chemical nature to the relentless inquisitiveness of modern chemists. They do differ from most other food constituents, however, in that their main function is neither to furnish energy nor building material, but to serve as chemical tools by means of which the cells of the body are able to do their work.

The general function of vitamins is much like that of the hormones of the body, but whereas the latter are "home-made," the vitamins have to be imported. Nevertheless, what is a hormone for one organism may be a vitamin for another. As vitamins they are not always imported in the active form in which they exist in the body, but may be altered or partially synthesized from mother substances in the food. The amounts required are so small that it has been found convenient to calculate them in millionths of a gram.

There started out to be only three vitamins, A, B, and C, but this simple A B C stage was very short-lived, and lasted only from about 1914 to 1920.

In 1922 the rickets-preventing vitamin D was shaken loose from A, under whose skirts it had been hiding, and at about the same time still another vitamin which had been hiding in the A complex was discovered. This one was found to be necessary for successful reproduction in rats; it was called the "anti-sterility factor X" by its discoverers, but was soon christened vitamin E. Between 1919 and 1926 the view progressed from a suspicion to a certainty that vitamin B also was not a unit. The old "vitamin B complex" has given birth to a whole litter of "B's," some of which have been dignified by separate letters of the alphabet (G, H, L, and M), while others have had to be content with numbers (B_1 to B_7), and still others, due to the hesitancy or conservatism of their deliverers, have merely been called "factors." One of the latest of this prolific family, the "P-P factor" which prevents pellagra, was so difficult to separate from some of the subnumeral B's that it was identified as a well-known chemical, nicotinic acid, before it was awarded a letter or even a number of its own, so it may never take the place which it well deserves in the vitamin alphabet.

Very recently the Hungarian scientist, Szent-Györgyi,

was awarded a Nobel Prize for the discovery of a new vitamin P which he believed to be distinct from vitamin C. More recent work indicates that vitamin P has no real existence.

A few years ago a vitamin K was added to the list, and recently some Japanese chemists distracted scientific if not popular attention from other Japanese pursuits by announcing two new vitamins, L_1 and L_2, said to be needed by rats to produce milk for their young. Only a few months ago monkeys, supplied with all the members of the B family known to be needed by human beings, still developed pellagra-like symptoms which were cured by Brewer's yeast or liver extract. The unknown factor was called vitamin "M."

The rapid multiplication of vitamins became so confusing that a special committee of scientific experts had to be set up to straighten out their names; but in spite of the committee a clear grasp of the true relations of the various members of the B group, at least, can only be acquired along with a good-sized headache, partly because one worker experimenting with chicks, another with rats, and another with dogs may find different effects from the same vitamin, different vitamins causing similar effects, and different effects caused by different dosages of the same vitamin. Professor McCoy of Cornell recently complained that the modern vitaminologist is afflicted with as many alphabetical vitamins as Job was with boils, and proposed that the League of Nations might set up a vitamin registry where each new or supposedly new factor for stimulating growth, or preventing skin sores, or what not, might be registered by number.

Now, however, things are getting better, at least in the B family, for B_1, B_2, B_6 (alias "factor I"), and the pellagra-preventing factors have all been positively identified chemically. Recently the "filtrate factor" of some writers, "factor II" of others, and "chick anti-dermatitis factor" of still

others, has been identified with pantothenic acid. Some relief is afforded by Dr. Cowgill of Yale who claims that B_3, B_4, and B_5 have no real existence.

Not all vitamins are needed by all animals, nor do they affect all animals in a similar manner. Man, monkeys, and guinea pigs, for instance, are the only animals known to require vitamin C; others presumably are capable of making their own, or harbor bacteria which do it for them. The nicotinic acid which prevents and cures human pellagra is not identical with the B_6 which prevents rat pellagra, and apparently the representative of the B family which prevents a skin disease in birds is different from either; as noted above, recent work indicates that the latter may be identical with pantothenic acid, a substance found in cells of all kinds of organisms from bacteria to mammals, and indispensable to all. For some organisms it is a home-made product, for others a vitamin. How we get ours is as yet unknown. There is reason to believe that thiamin (B_1) and nicotinic acid are likewise universally needed substances. This appears not to be true of some of the other vitamins.

There are at least ten different kinds of vitamin D, not all of which are equally effective in rats and chicks, and no one actually knows how they might work in lizards or earthworms, if needed at all. It is generally thought that rats and man have much in common nutritionally—any food handler will agree to this! Therefore, until evidence to the contrary comes to light, it is assumed that what is necessary to keep a rat hale and hearty is also necessary for *Homo sapiens*.

The vitamin potency of various food substances was until recently determined by a "biological assay" method; a diet was prepared containing adequate quantities of all food requirements except the vitamin to be tested. This was fed to rats (or other experimental animals) until they began to

show symptoms of deficiency. They were then treated to the same diet *plus* varying amounts of the foods to be tested. The smallest amount which would cause certain minimum improvements in growth or other effects was called a unit. Not all nutrition workers originally used the same units, but the Health Organization of the League of Nations brought order out of confusion by adopting standard "international units."

As the pure chemical substances which constitute the vitamins are discovered, one after another, weights of these pure substances are substituted for the standards of reference originally adopted. The weights are best expressed in micrograms (one one-millionth of a gram). The present international unit of vitamin A is equivalent to 0.6 micrograms of carotene, of B_1 to 3⅓ micrograms of thiamin, of C to 50 micrograms of ascorbic acid, and of D to 0.025 micrograms of crystalline vitamin D. No international units of other vitamins of the B group or of E or K have yet been proposed. The older units of vitamin B_2 or G were based on the whole complex, before riboflavine, nicotinic acid, and others were segregated.

It is still necessary to test for most vitamins by the laborious and tedious "biological assay" method, but simple chemical tests are being discovered. A few years ago if some inquisitive person wished to know how much vitamin C there was in a new variety of apple, he would have had to play dietetic nursemaid for a half-dozen pens of guinea pigs for three months, and then perform careful autopsies on them, whereas now he can obtain the same information in a few minutes with a test tube and some chemicals.

There has been so much talk of vitamins in recent years that people have become very vitamin-conscious. Food and drug manufacturers, as might have been expected, were

quick to cash in on this interest and to help it along, as they have many other popular interests, by large-scale advertising. Foods are often advertised as containing this or that vitamin when an average human portion of the food would contain barely enough to satisfy a mouse. Drugstores have found concentrated and purified vitamins almost as much a gold mine as are cathartics and liver tonics. Many of the ideas fostered by drug manufacturers have proved to be pure fads, and there has been a large body of conservative-minded citizens among us, including many in the medical profession, who felt that the use of supplementary concentrated vitamins was neither necessary nor desirable. They remembered that people were able to remain in at least an apparently good state of health hundreds of years before vitamins were dreamed of, and that some of our more primitive "poor relations" in Africa and Central Asia who haven't yet dreamed of vitamins seem to be just as hale and hearty as the consumers of drugstore concentrates.

But time marches on at a faster gait in our civilized communities than in primitive ones, and there have been far greater changes in our diets, our work, and our recreation. We use larger amounts of high calorie foods, such as sugar, white flour, polished rice, and lard, from which we have extracted all the vitamins; we subject other foods to storage, cooking, crushing, or other manipulations which at least partly destroy the vitamins we haven't extracted; we throw away the outer parts of vegetables and the blood and many special organs of the animals we eat, thereby eliminating the parts especially rich in vitamins; we have circumvented Nature's plan for letting us produce vitamin D in our own sun-tanned skins by introducing into our lives such things as smoke palls, clothing, windows, and indoor occupations. We have surrounded ourselves with labor-saving devices which

make us less physically active, thus reducing the amount of food we consume and incidentally the quantity of vitamins. Even if we eat an abundance of foods known to contain vitamins, and stuff ourselves with the fruits and vegetables that health enthusiasts are constantly recommending to us, unless our selection is carefully made, we could very easily fall short of the amounts of vitamins which are now considered ideal for perfect health.

A few years ago, before we knew what large quantities of vitamins a human body would use if they were available, and before we had any very easy or accurate methods of determining the actual amounts of different vitamins in our foods, it was still thought that common foods could be relied upon to supply us with all we needed, even if we ate a normal amount of the devitaminized foods which play such a prominent part on modern dining tables. Actually, a person eating an ordinary mixed diet with a large amount of sugar and white flour, with a fair amount of milk, butter, whole cereal, vegetables, and fresh fruits, would never suffer from beri-beri, pellagra, scurvy, or diseased eyes, or become a dwarf. He would probably consider himself in good health, because he was in as good health as the average of his neighbors. He probably wouldn't consider it anything but natural if he had fairly frequent colds, had unhealthy teeth and gums, had a little difficulty in adjusting himself to seeing in the dark, had a not-too-good appetite, was frequently afflicted with a tired feeling and headaches, was subject to gassiness and constipation, occasionally had fits of gloominess and depression, and was inclined to have a tantrum if his wife inadvertently passed a forcing bid in a bridge game.

On the other hand, it has been shown repeatedly that when more abundant vitamins are taken, a state of "superhealth" is achieved. What most of us consider normal

health is actually not the best that we could have. Ill health from such common causes as unhappy relations with one's wife or with the stock market, or poor digestion, is sometimes improved to an astonishing degree. Many a case of poorly defined ill health blamed on heritage or the inscrutable will of the Lord is due to nothing more than insufficient vitamins in our daily bill of fare. A recent report on treatment of hardening of the arteries and accompanying diseases of the blood-system and kidneys showed that a high proportion of them responded better to large doses of vitamins and minerals than to any other form of treatment. Many cases of chronic arthritis are similarly benefited.

Julian Huxley said that if he were able to dictate the food habits of a nation for one generation, he could add one cubit to their stature and double their resistance to disease. British medical authorities have gone so far as to say that 99 per cent of the so-called common illnesses are directly or indirectly due, at least in part, to vitamin deficiencies.

There is reason to believe that generous supplies of vitamins and minerals, such as would be obtained either by a careful and intelligent choice of natural foods, or by the use of supplementary vitamins, would increase the expectancy of life from the seventy years that were awarded to our ancestors, to seventy-seven. Lest anybody still far removed from that age might not fully appreciate what an asset that would be, he should pause to think that the added seven years is merely a visible proof of a 10 per cent better life throughout the preceding seventy, and that the man who has extended his span of years to that extent had the vim and vigor of forty-five when the family Bible said he was fifty.

Of course there are many other causes of poor health than inadequate vitamins, and vitamins alone cannot make a man well who is suffering from an infectious disease, or

glandular disturbances, or a cancer. Yet even in such conditions extra vitamins may be of great benefit. Extra vitamin B is required when the metabolism is stimulated by an overactive thyroid or by fever, and extra vitamin C is needed when the toxic products of infection, metal poisoning, etc., combine with large amounts of it and take it out of circulation.

Yet disease nearly always leads to lowered rather than heightened intake of vitamins. Many diseases have a toxic, exhaustive effect on the nervous system, leading to insomnia. Recent experiments show that all ordinary types of insomnia are helped by large doses of either vitamin B or vitamin C, or both. These vitamins have been hailed as ideal sedatives for alcoholics suffering from delirium tremens, for hyperthyroid patients worn down by their overactive glands, for elderly people sleepless because of hardening arteries in the brain, and for convalescents from operations or debilitating diseases. Vitamin treatment which gets at the fundamental causes of insomnia is a great advance over the older method of merely masking symptoms by the use of stupefying drugs.

It is obvious that human vitamin deficiencies are nearly always multiple in Nature. Pure dietary deficiencies can be produced experimentally in animals by the careful and laborious preparation of a diet containing enough of all necessary food substances except one vitamin or mineral. But even when conscious efforts are made to obtain a single deficiency it is very difficult to do. When foods are withheld to eliminate one vitamin, others are often found to have been eliminated also. Few human foods contain single vitamins, so it is extremely likely that any diet or condition which results in such extensive deprivation of one vitamin as to produce clear symptoms of its lack, will at the same time be lacking in other vitamins, though possibly to a

milder degree. Any condition which interferes with the absorption of vitamin A, for instance, is also liable to interfere with the absorption of other fat-soluble vitamins. Any diet lacking in one constituent of the vitamin B complex is also liable to be deficient in others. The amazing results recently obtained by treatment of pellagrins with nicotinic acid fall short of complete cure unless some vitamin B_1 is provided also. The symptoms due to one deficiency may so overshadow those due to others that the latter escape notice, but in all such cases treatment with a single pure vitamin is almost sure to fall short of a complete cure.

To sum up, the vitamins known or believed to be necessary for normal human health, with modern ideas of the amounts necessary, are as follows:

Soluble in fats:

A, a derivative of carotene; needed for normal growth, healthy eyes, and resistance to infection. Normal daily needs from 3000 units in infants to 6000–8000 in adults and 9000–10,000 in expectant and nursing mothers.

D, irradiated "sterols"; needed for proper calcium and phosphorus metabolism, to produce healthy bones and teeth, and to prevent rickets. Normal daily needs for children in first year 800–1200, in second year 800, thereafter gradually less.

E, an alcohol, tocopherol; needed for normal reproduction in rats, and probably in man also. Normal daily needs unknown, but small except during pregnancy.

K, a naphthoquinone; needed for production of prothrombin, to facilitate the clotting of blood. Apparently needed by man only in unusual circumstances.

Soluble in water:

B_1, thiamin; needed for healthy nerves, good appetite, and normal metabolism of carbohydrates; prevents beri-beri. Normal daily needs, 100 units in infants, 300–600 in adults, 400–800 in expectant and nursing mothers.

B_2, or G, riboflavine; needed for normal growth in rats, and for continued health in dogs, but little is known about its effects in man. Aids in metabolism of carbohydrates and proteins. Normal daily needs unknown, possibly 10–30 units.

P-P factor, nicotinic acid; needed for prevention of pellagra and sprue. Normal daily needs unknown, but very small.

C, ascorbic (or cevitamic) acid; needed for healthy teeth, normal development of supportive and connective tissues, and resistant capillaries; prevents scurvy. Normal daily needs, 100 units for infants, 200 for adults, and 400 for expectant and nursing mothers.

II

VITAMIN A

BACK at least as far as the time when the children of Israel entered the Promised Land and the Egyptians were building the Temple of Ammon at Karnak, night blindness and tearless, inflamed eyes, the most characteristic symptoms of lack of vitamin A, were known and described. Four centuries before the Star of Bethlehem exerted its guiding power, astute old Aristotle, the Father of Medicine, not only referred to night blindness but mentioned that it could be cured by eating liver. From time immemorial, in periods of famine, war, or isolation from dairy products or green vegetables, men have suffered from vitamin A deficiency. One of the most severe outbreaks in recent years occurred in Denmark during the World War. Food was scarce and prices of necessities as well as luxuries were heading for the stratosphere, but Denmark had an abundance of dairy products which were in such demand by her warring neighbors, and brought such high prices, that the export of butter kept the whole country in bread and clothes. But like the justly celebrated offspring of a shoemaker, the children suffered—they had to subsist on skimmed milk. After a year or two of this, eye troubles, respiratory diseases, skin infections, and stunted growth swept the youth of the land like a plague. When the cause of the trouble was detected, it was promptly remedied, and the children quickly returned to the exuberant state of health which they usually enjoy in a country blessed with milk and butter.

The existence of vitamin A was discovered a quarter of a century ago by two pairs of scientists in the same summer—McCollum and Davis at the University of Wisconsin, and Osborne and Mendel at New Haven. In 1932 England's Professor Drummond concentrated a sticky yellow oil from halibut livers which he thought was nearly pure vitamin A, but it was near the end of 1936 before Dr. Holmes, at Oberlin, finally obtained the pure crystalline substance. It is 50 per cent again as potent as Professor Drummond's thick oil; one gram of it contains three million units. Recently Dr. Hickman of the Eastman Kodak laboratories, by a clever process of "vacuum distillation," has developed a method by which pure vitamin A (and also vitamin D) can be produced at about the cost of a good grade of brandy. He has erected a plant which will produce sixty billion units of vitamin A per week, and hopes to treble that by improved stills now under construction. The vitamin, flavorless and pure, becomes available for mixture with such foods as butter, margarine, or chocolate. The curtain may be falling on the era of crude fish liver oils!

Vitamin A is a fat-soluble substance formed in animal bodies from a chemical cousin called carotene, found in plants. Carotene is deep yellow in color, but it is abundant not only in such yellow-colored vegetables as pimientos, carrots, sweet potatoes, and yellow corn, but also in the green parts of plants. It is only made in sunlight and so is most abundant in thin green leaves; it is about thirty times as abundant in the green outer leaves of a head of lettuce as in the pale heart. It is very abundant in parsley, endive, chard, spinach, and other edible greens, and also in alfalfa and grass. Fruits, with the exception of apricots, are less rich in it, and most grains, starchy tubers, and nuts have negligible amounts.

Vegetable-eating animals obtain their vitamin A in the form of the yellow carotene found in plants, while carnivorous animals usually get it from other animals directly as vitamin A. If taken in as carotene, it is at once converted into vitamin A in the liver, unless there is a large excess. The body has considerable storage capacity for vitamin A, and is generally believed to be able to do without a fresh supply for a long time without suffering, if previously there was an abundance. This may be true so far as severe symptoms are concerned, but recently Dr. Jeghers of the Boston University School of Medicine, after putting himself on several times the necessary daily dose of the vitamin for a number of weeks, cut his intake down to only about one-twentieth of the normal adult requirement. Within a week tests showed lowered ability to see in the dark, and in about a month he had well-developed night blindness. Nevertheless, there is no doubt but that a good excess of vitamin A during the summer months helps to tide people over a long winter season when the supply of the vitamin may be diminished.

There is also evidence that a liberal allowance of this precious substance early in life may have effects, such as well-formed teeth and resistance to infection, which may last throughout life. In other words, what a child eats when he is three years old, possibly even more when he is three months old, has an influence on his health when he is in his "teens." Nature recognizes this; her "survival of the fittest" method of seeing to it that animals do what is best for their kind has provided all young birds and mammals with term health insurance in the form of a fixed vitamin A tax on the parents, deducted at source and deposited in the yolk of eggs and the cream of milk. Even if a hen or a cow has to deplete her own resources of vitamin A to a dangerous extent

to do it, Nature sees to it that she sets aside an adequate amount for the welfare of her young.

This offspring insurance has been a tremendous boon to the human race, for the domestication of cattle and chickens has provided us with a very easy method of getting the carotene of alfalfa, grass, and other greens separated from the roughage to which it is bound, and made available in a concentrated, edible, and palatable form. Milk is undoubtedly the most important single source of vitamin A for most children and many adults, but eggs are a close second. Aside from milk and eggs, and such dairy products as butter and cheese, liver is also important among animal products, since this is where animals store most of their vitamin A. Milk and eggs fluctuate in their vitamin A content according to the food of the animals or birds producing them, but liver is even more variable since its content depends on the excess the animal has for storage. Some fishes store up amazing amounts of both vitamin A and D in their livers, although the amounts of each of these is by no means parallel in different kinds of fish.

Because of its amazing ability to store up vitamin A in its liver, the halibut has come to be one of the most prized denizens of the sea. It is a huge, flat, crooked-eyed, voracious creature living in the depths of cold northern waters. It captures fish and other sea food either by lying in ambush half-buried in the sand, or by active pursuit, stunning codfish and haddock by blows from its powerful tail. The vitamin A which the halibut and other deep-sea fishes so assiduously collect is probably first manufactured as carotene in microscopic marine algae, then converted into vitamin A by the myriads of small crustaceans and other minute drifting animals, and then successively concentrated by small surface fish, larger cod and haddock, and finally by tunas and hali-

but. The millions of units of vitamin A in the liver of a 150-lb. halibut may be the accumulated "take" of twenty-five years of predatory habits.

Fat fish, such as salmon and sardines, provide vitamin A in their flesh as well as in their livers. Oysters, too, are a good source. Although vitamin A is likely to be where the fat is, especially in fishes, there is no correlation between the amount of fat and the amount of stored vitamin A, whether in fish, milk, or human beings. As compared with fish, land animals are very poor collectors of vitamin A. The liver oil of the relatively inefficient cod has from twenty to fifty times as much vitamin A per gram as butter, while that of the halibut has over a thousand times as much.

Vitamin A is not one of the delicate vitamins which are shorn of their power by cooking or preservation. The parent substance, carotene, is even more durable than vitamin A; it is seldom damaged by processes of cooking or canning, although exposure to air at high temperatures has some deteriorating effect upon it. Stored vegetables exposed to warm air, or allowed to ferment, gradually lose some of their carotene potency. For this reason frozen fruits and vegetables, now becoming available by a quick-freezing method which saves them from the injurious effect of large ice crystals in the cells, are likely to have more vitamin A than "fresh" vegetables in a market. Even cooked or canned vegetables may be slightly better.

Vitamin A has two widely different uses in the body. It is a constituent of the light-sensitive pigments in the retina of the eye upon which our vision depends, and it serves as a chemical tool for the normal activities of body cells, particularly epithelial cells.

It has long been known that the rods of the eye are coated with a reddish-purple pigment—called visual purple—that

functions like the silver preparation on a photographic film, being decomposed by even very dim light. This chemical change gives rise to a nerve impulse that causes the sensation of light, and it is on this mechanism that our ability to see in dim light is based. Since the visual purple is a combination of vitamin A and a protein, a deficiency of vitamin A interferes with the production of this substance and consequently with vision at night.

The more visual purple we have, up to a certain maximum, the dimmer the light in which we can see, and the more vitamin A we have, the more rapidly visual purple can be regenerated after it has been decomposed by bright light. People deficient in vitamin A find difficulty in driving a car at night, are unable to see faint stars, and sit in other people's laps when getting seated in a darkened theatre.

Blindness following exposure to the glare of headlights at night is due to decomposition of visual purple by the light, and its duration depends on the speed with which the pigment can be replaced. In a normal individual this takes only a few seconds, but in one suffering from lack of vitamin A it takes much longer, and a fast-traveling car may have to be driven hundreds of feet in complete blindness. Many a wrecked car and broken body would be spared if parents as well as children would eat more spinach, or put more butter on their bread.

When the vitamin A deficiency is mild there is often no consciousness of reduced night sight, but there are delicate tests by which even very slight abnormality can be detected. The use of these tests has demonstrated an amazing and unsuspected prevalence of insufficient vitamin A even in typical American communities. A recent investigation of a series of children in Iowa showed defective ability to see in the dark in 26 per cent in rural schools, 53 per cent in a county seat

of 2000 population, and 56, 63, and 79 per cent, respectively, in the upper, middle, and lower economic levels in a city of 150,000. Of seventy-eight of the defective children who were given three teaspoonfuls of cod-liver oil daily (to supply vitamin A) only three failed to improve, and the majority were normal in from four days to a month. Even more striking was a recent survey by Dr. Jeghers of 162 students in the Boston University School of Medicine. Fifty-five were below normal in ability to see in the dark. The following table of comparison with normal students is enlightening:

	Students with normal night vision	*Students with impaired night vision*
Ate at home	74%	42%
Ate in restaurants	16%	32%
Ate in quarters	10%	26%
Those eating in quarters averaged weekly	$4.20	$2.80
More than one full meal per day	100%	40%
Average duration of colds	5.5 days	7.4 days
Total number of days of illness	47	136

The students with inadequate vitamin A were more frequently those eating away from home, spending too little on their food, and subsisting on doughnuts and coffee for breakfast, and sandwiches, sodas, etc., for lunch. About half of the defective students were conscious of their night blindness—they sat in other people's laps when getting seated in a darkened theatre, and were unable to drive a car at night except on lighted streets. A third of them also complained of dryness of the skin, and three of dry eyes. Several

noticed that their annoyance from dry skins disappeared after a summer at home with mother's cooking.

Another recent investigation was made in an Ohio yarn factory, where the employees complained of eyestrain; they couldn't read after a day's work, their eyes smarted and burned, and they made too many errors in color matching. After three capsules a day of carotene in oil their mistakes decreased by 75 per cent, they had far more eye comfort, and in many cases their general health improved.

Until very recently the mechanism of daylight vision—with which the cones of the eyes are concerned—was unknown, although many similarities between the behavior of rods and cones suggested a similar mechanism for both. In 1937 it was shown that the cones also possess a light-sensitive pigment, though it is very dilute, and that this pigment—called visual violet—is also dependent upon vitamin A. Vitamin A is therefore an important factor in day as well as night vision.

The other evidences of vitamin A deficiency, which fortunately are not striking when the deficiency is slight, are due to obscure effects on the normal activity of body cells, particularly the epithelial cells. Rats which are fed on a diet that has everything except vitamin A stop growing as soon as their stored vitamin is used up, lose vigor, become susceptible to infections, especially of the respiratory system, skin, and intestine, develop dry, sore eyes which finally become blind, and are prone to develop kidney stones. Recently early-developing injury to nerve cells and fibers has been observed in various animals, followed by such effects as paralysis and lack of muscular control. Female rats have their sexual cycle disturbed, and males, ceasing to produce sperms, become sterile. The teeth during growth have their enamel improperly developed. There is every reason to be-

lieve that all of these symptoms would develop in human beings as well if no vitamin A were supplied, but with more moderate deficiencies the injuries are often so indefinite as to escape realization. Vitamin A is used up in considerably larger amounts by growing children than by adults, and it is rapidly depleted in septic infections such as pneumonia, sinusitis, appendicitis, etc.

This epithelium constitutes the first line of defence against invasion of germs. It forms a stratified, resistant layer of horny cells in the skin; ciliated cells for sweeping dust and germs out of the lungs; a delicate, transparent film over the eyes; mucous cells to moisten the alimentary canal; secreting cells in all sorts of glands; sperm-producing cells in the testes; enamel-depositing cells in the developing teeth; etc. In the absence of vitamin A all the epithelial cells except those of stomach, intestine, and kidneys fail to become specialized for their particular parts, and tend to form flat, horny cells like those of the skin, which is often very inappropriate and undesirable. Even in the alimentary canal the mucus-producing goblet cells become greatly reduced in number, and there is evidence that these cells are instrumental in protecting the intestine against parasites. In the eyes the delicate conjunctival membrane which covers the exposed surface is normally kept moist and clean by a film of oil and a constant flow of tears; without vitamin A it becomes dry and dirty, the lids swell and become scabby, and pus flows instead of tears. When the deficiency in vitamin A is severe, the dry, inflamed condition of the eye leads to infections which may cause blindness. There are thousands of cases of blindness of this type in India and Africa.

In the respiratory system defective epithelium allows germs to get a foothold, and disease follows—colds, sinus troubles, bronchitis, middle ear infections, etc. When peo-

ple who have been getting along on too little vitamin A are given an adequate amount they often notice a marked difference in the number and duration of colds. In the alimentary canal insufficient mucus secretion leads to ulcers, erosion, poor absorption, and diarrhea. A poor grade of epithelium in the genital organs leads to delayed menstruation, miscarriages, or failure to produce sperms. An extra amount of vitamin A during the last month of pregnancy reduces the chance of mild infections following childbirth. Pregnancy and breast feeding drain away reserves at a rapid rate, and this is also true of the changes at puberty; rats on poor vitamin A diets are very likely to get lung diseases just as they are maturing, and it may be more than coincidence that human beings, too, are especially likely to "go into a decline" with consumption soon after puberty.

When the teeth are forming, some epithelium which sinks below the surface of the gum assumes the specialized function of taking up minerals and depositing them as a veneer of enamel over the underlying dentine; without vitamin A these cells fail to become specialized as stone masons, and the enamel does not form normally; even the underlying dentine is abnormal because the dentine cells seem to be organized and directed by the enamel organ covering them. Vitamin A deficiency during the period of tooth formation probably does even more than lack of vitamins C and D to plague us with soft, easily decayed teeth. Kidney stones, too, are associated with vitamin A deficiency: in a recent investigation in Philadelphia twenty-four of twenty-five kidney stone patients showed evidence of inadequate vitamin A by their night blindness, although most of them failed to improve when treated with vitamin A. It was believed their deficiency was due to an abnormal inability to assimilate or make use of the vitamin. It is claimed that a diet rich in

vitamin A sometimes causes kidney stones to redissolve. Kidney and bladder stones, as well as blindness, are very common in Northern India where milk and butter are scarce, and the climate too austere for growing much besides grain.

When the only evidence of vitamin A deficiency is a slight lowering of ability to see in the dark, an improvement of the diet to bring the vitamin intake up to normal is all that is required, but when noticeable symptoms have developed it is best to take large daily doses until a normal condition is reached, which may require several weeks. There has been considerable difference of opinion as to what human requirements of vitamin A are, but recent use of the "biophotometer" to measure normality of sight in dim light indicates that a daily intake of 4000 to 5000 international units (2.4 to 3 milligrams) is close to the minimum for normal adults, whereas growing children require relatively larger doses. Professor Mary Rose, of Columbia Teachers College, suggests 280 units per 100 calories in the diet for growing children, which would make it range from about 3000 units in a child under a year old to over 8000 at puberty. For pregnant and nursing women a daily intake of 8700 units has been recommended by the League of Nations Committee on Nutrition. There are some who think that even this is not generous enough, yet an investigation in a Massachusetts hospital out-patient department showed that less than one in ten of such women were getting over 7000 units per day. In England a few years ago a significant decrease in sickness among pregnant women was observed following the administration of cod-liver oil, and it was believed that the vitamin A was the effective ingredient in the oil, the vitamin D having very little to do with it. It would be excellent insurance if all expectant or nursing mothers would take daily a teaspoonful of cod-liver oil, or better still a few drops of hali-

but-liver oil, to provide the extra vitamin A they need. This will supply about 3000 units, a quart of milk will provide 1500 to 2000 more, and the rest will come mainly from other dairy products, eggs, and green or yellow vegetables.

It should be kept in mind by vegetarians that carotene is not as completely absorbed from the intestine as is the vitamin A of dairy products, eggs, liver, or fish oils. A recent investigation in India showed that from 35 to 55 per cent of the carotene of the food passed out of the body in the feces, whereas every bit of the vitamin A was utilized. In cases of jaundice, where bile is missing from the intestine, carotene, like fatty acids, fails to pass the border patrol and is wasted (also true of vitamin K and probably E), whereas the converted vitamin A is admitted on its own passport. Mineral oils interfere with absorption of carotene much more than of vitamin A by dissolving it and carrying it out of the body. Vitamin A is said to be injured by contact with iron salts or rancid fats.

There is no danger of overdosage with carotene or vitamin A. Doses of 100,000 units a day are sometimes given in cases of extreme deficiency. If a great excess of carotene is absorbed it is deposited in the subcutaneous fat and gives the skin a golden glow, but it does no harm. In a milk-producing animal excess carotene is also excreted in the milk, giving it a yellow color, but the yellow color of cream and eggs is no indication of its vitamin A value, for there are other causes of deep color, especially in eggs, and even very pale cream or eggs may be rich in colorless vitamin A.

III

THE "B" FAMILY—VITAMIN B_1, MOTHER OF THE "B" FAMILY

NO animal on earth except man, and on rare occasions the animals which he has made dependent upon him for food, suffer from lack of the vitamins which were formerly grouped together under the letter "B." The vitamin which is now known as B_1, particularly, is so widely distributed in natural foods that only the diabolical ingenuity of man could develop a diet seriously lacking in it. But at least twenty-six hundred years ago man's ingenuity accomplished this very thing. In many parts of the Orient the human animal restricted his agricultural efforts largely to the production of rice, and then developed a method of improving the rice for his consumption by polishing it, i.e., removing the outer coat and germ. In so doing he incidentally removed all the vitamin B_1, which is richly present in the polishings. From that day to this, beri-beri has been one of the principal scourges of mankind in southeastern Asia, and it is no mean distinction to be a principal scourge in that hotbed of human scourges.

In 1879, human beings discovered another process by which to deprive themselves of vitamin B_1—the making of white flour. However, white flour rarely forms nearly so large a part of the diet as is the case with rice in some parts of the world, so the elimination of the wheat germ with the bran was not so serious a matter. Bread may be the staff of life, but fortunately it is not often too exclusively leaned

upon as a support. However, there are exceptions. Beri-beri is not uncommon in northern parts of Labrador and Newfoundland where the menu is made up mostly of white bread, molasses, and salt pork. In 1910 a ship ran ashore up there and lightened its cargo by unloading a large amount of whole wheat flour, with the result that beri-beri disappeared from the region for a year.

In the Japanese navy back in about 1880, one or two out of every five men were sick with this disease. On one ship 195 out of 350 men were down at one time. A brilliant Japanese naval officer concluded that the disease was due to an inadequate diet, and to prove his point he was permitted to experiment with two training ships. Both were sent on a long cruise occupying about nine months. The regulation diet was provided on one of these ships, while a better one was allowed on the other. The ship with the regulation diet had 169 cases of beri-beri and 25 deaths in a crew of 276. On the other ship there were only 14 cases and no deaths.

A few years later, in 1897, Dr. Eijkman, a Dutch scientist in Java, observed in fowls fed on polished rice a disease which he believed was similar to beri-beri, and showed that rice polishings contained something that prevented the disease. He had a survey made of the jails in the Dutch East Indies and the report showed that of every 10,000 prisoners fed on polished rice 3900 had beri-beri, while of those fed on unpolished rice there was only 1 case in 10,000. The fact that the diet was to blame and not an infection, as many believed, was conclusively proved by taking 300 laborers into the jungle where no infections from other human beings could reach them, and where they could be isolated from the unsanitary conditions prevailing in the native villages and on estates. Half of them were put on a diet of polished rice, the other half on less refined food. In three

months beri-beri broke out in the group fed on polished rice while the other group remained healthy. The diets were then reversed, whereupon the group with beri-beri recovered and the group which was formerly healthy became afflicted by it.

About this same time the Americans took over the Philippines and were justifiably shocked at the unsanitary conditions and poor food of the Manila prisons. They killed off the vermin, provided decent sewage disposal, laundered the clothing, and among other improvements in the diet provided clean, white, polished rice instead of the coarse, brown, unhulled rice formerly provided. The result of their well-meant efforts was a severe outbreak of beri-beri that more than nullified all the other benefits. Another example of unexpected disaster from well-meant reform occurred when the League of Nations placed a certain Polynesian island under the mandate of Australia after the World War. The natives, it seems, were prone to indulge in a (to them) delectable alcoholic beverage prepared from yeast. The august and motherly League of Nations felt that so prevalent a state of merriment as existed on the island was unbecoming in a people for whose moral and physical welfare the League was responsible, so it stopped the practice. With the decline of inebriety there was an outbreak of beri-beri, and as in other prohibition experiments the law had to be modified. With the re-introduction of not-too-long-fermented toddies for the mothers the infant death rate fell from 50 to 7 per cent. Still feeling the need of prohibiting something, the government of the island then prohibited white flour and polished rice instead of the cup of cheer, and got better results.

About 1919 suspicions began to arise that vitamin B as then known was in reality a composite of several vitamins,

but it was not until 1926 that the splitting up of the "B family" really began. From that time until the present more and more different offspring from old mother "B" have been shaken loose from the enveloping folds of her skirts. The discovery and identification of these "B" offspring has been a very complicated detective story, to the solution of which many scientists have contributed. Not all the "discoveries" have maintained a place in the esteem of nutritionists, but a number of them have stood the test of time.

Fourteen years after Funk had obtained his anti-beri-beri extract from rice polishings and yeast, vitamin B_1 was obtained in pure form, though in very minute quantities, in the same laboratory in Java where beri-beri was first shown to be due to a deficiency in the diet. Later Dr. R. R. Williams, of the Bell Telephone Laboratories in New York, improved the technique so that larger amounts could be obtained for study, but it still required about two and a half tons of rice polishings to extract one ounce of the pure vitamin. After twenty years of research, in the course of which the molecules of the vitamin were chemically taken to pieces bit by bit to find out what they were made of, and then pieced together again like the parts of a jigsaw puzzle, Dr. Williams finally, in 1936, solved its chemical structure and succeeded in making it synthetically. Now the pure crystalline substance can be obtained in any drugstore at a cent or two per milligram, and 1½ to 2 milligrams per day is all an average man requires. There would be no difficulty in carrying home a year's supply; the equivalent in weight of two aspirin tablets would be more than enough.

The name "thiamin" has been approved for this pure chemical substance. It is water-soluble, and differs from all other vitamins, except the other members of the "B" family, by containing nitrogen. It appears to be one of Nature's

earliest inventions in the evolution of life. It is probably present and necessary in all living things, although the quantity, except where it is especially stored, is usually less than one part in a million. It is necessary for bacteria, fungi, green plants, and all kinds of animals, from amoebae to whales.

Without thiamin, respiration in living organisms is interfered with; the burning of carbohydrates to provide energy cannot go on in a normal manner. The rich deposit of thiamin in the germ of starchy seeds is clearly a provision on the part of Nature to enable the germinating plant to use the starch for energy with which to grow until it can spread its leaves to the sun, whereupon it is able to manufacture more thiamin for its continued use. As Dr. Williams has said, man commits a crime against Nature when he eats the starch from the seed and throws away the mechanism necessary for its utilization. The starch without thiamin is like a safety match without the scratching surface.

Green plants, and many fungi, yeasts, and bacteria are able to manufacture thiamin, but no higher animals are capable of doing so. Green plants make it only in the upper parts, not in their roots, so no root growth is possible without a supply of thiamin either from a supply stored in a seed or from the green portion of a plant. A recent study showed that when root-tips are removed from their parent plants they fail to grow in a plain solution of sugar and mineral salts, but grow well if there is added one part of thiamin in 500,000,000,000 parts of the culture medium. Soaking roots of transplanted plants in a dilute thiamin solution keeps them from wilting, and watering them with it stimulates growth.

In cuttings, the green parts supply enough thiamin to start meager root growth, but much more rapid growth is

stimulated if minute amounts of thiamin are added to the soil or water. This is the reason why cuttings grow better if they are split at the bottom and an oat seed inserted.

Most animals, including man, depend upon outside sources for their thiamin, but some, such as cattle, harbor bacteria in the rumen of the stomach which make it for them in their own alimentary canals. It is for this reason that cow's milk always contains a fair amount of thiamin regardless of the diet, which is not true of human milk. In the Philippines, for instance, mortality from beri-beri is particularly high in breast-fed infants.

The potency of various foods in vitamin B_1 has been measured by various methods of "biological assay." A method which was formerly extensively used was to determine the amounts of a particular food which, if fed daily in addition to a diet entirely lacking in vitamin B_1, would enable rats which had been depleted of the vitamin to make a certain very slight gain in weight each week for two or three weeks. This amount of the food was said to have one Sherman unit of vitamin B_1. In the last few years better methods have been developed. Rats are depleted of the vitamin until they shows signs of polyneuritis. They are then given a test dose of a known quantity of pure thiamin. They recover in a few hours and are then watched to see how many days elapse before the symptoms return. They are then given a certain amount of the food to be tested and the curative effect compared with that produced by thiamin. On the basis of the results obtained smaller or larger doses are given after the rats have relapsed again, until finally the quantity equalling the dose of thiamin is reached. Some assayers prefer to use the rate of the heart beat as a criterion. After two weeks of vitamin B_1 depletion a rat's heart slows from 500 beats per minute to 250, and a dose of thiamin brings it back to nor-

mal for several days. The method is a good one except that it requires an expensive electrocardiograph.

In the last few years other methods of testing for thiamin in blood, urine, and foods have been developed. One method is to find how much of the tested substance is needed to supply enough thiamin to allow a certain mold to grow in a thiamin-free sugar solution. Another is to test its effect on production of alcohol by yeasts. As little as one-millionth of a gram can be detected in this way. There are chemical color tests which are useful in studying body saturation, excretion, etc., but they have not yet been very extensively used for the testing of foods. It is difficult to extract all the thiamin present in foods, and it is doubtful whether even the body accomplishes this during digestion, so the actual vitamin B_1 activity of a food still has to be tested by biological assays on rats, pigeons, or other animals.

The international unit of vitamin B_1 is based on the biological activity of a certain amount of a standard extract of rice polishings adsorbed on Fuller's earth. The unit is equivalent to about $3\frac{1}{3}$ micrograms (.0033 mg.) of thiamin. Sometimes "Sherman" units are found on labels; roughly a Sherman unit equals 2 to 3 international units.

Unlike vitamin A, thiamin is stored in the body in rather limited amounts, the largest reserves being in the liver, kidneys, pancreas, and heart. For this reason it is even more important than with most vitamins that the required amount of thiamin be included in each day's food.

Although vitamin B_1 is very widely distributed in Nature, it cannot be said to be *abundant* in any common foods. There is no single food that can be relied upon to supply the major part of a day's requirement. Even the richest sources contain only 20 to 30 parts per million by weight, and most common foods not more than from 0.1 to 4 parts per mil-

lion. It is about 100 times less abundant in foods considered rich in it than is vitamin C in foods in which *it* is rich. On the other hand, very much smaller amounts are required, it is more widely distributed in common foods, and it is not nearly so easily destroyed.

Two to three pounds of food averaging one part of thiamin per million would cover human needs. Such foods supply about 7 units per ounce. The only common foods which average more than 20 units per ounce are various whole grains; liver, heart, and kidneys of various animals; bacon, ham, and sausage among pork products; egg yolk; malted milk powder; green asparagus, string beans, dried beans, lentils, peas, and parsnips among vegetables; and various nuts. Whole wheat bread supplies just about 20 units per ounce, rye bread slightly less. From 7 to 20 units per ounce is afforded by lean meats and fish, whole eggs, milk, and a large variety of vegetables and fruits.

Although the actual content of vitamin B_1 in most fruits is relatively low compared with that of whole grains, nuts, and some vegetables, fresh fruits are nevertheless an important source because of the quantity in which they are eaten and the fact that they are eaten without any cooking or other manipulation which might reduce the vitamins they contain. Yeast is particularly rich in thiamin, but the amount of yeast used in making bread is too small to be of any significance. Wheat germ contains the entire daily requirement of a human being in half an ounce. Prepared bran is only one-fifth as rich in thiamin as is the germ. Oats also contain a relatively large amount.

Polished rice, white flour, and degerminated corn meal and hominy have almost none, but when rice is soaked and parboiled before being milled, the thiamin and phosphorus soak into the starchy part from the hulls and are thereby

saved. This has been a boon to the rice-eating millions in the Orient. Children in Indian institutions still suffer from riboflavine deficiency but they no longer have beri-beri. Pure sugars and starches are entirely lacking in thiamin, and no fats, even butter, contain important amounts of it. Beer, although sometimes advertised as containing vitamin B_1, has a negligible amount.

According to Dr. Sherman of Columbia, one of our leading vitamin investigators, if half the needed food calories are taken as fruits, vegetables, milk, and eggs, and if half of whatever breadstuffs and cereals are used are taken in the whole-grain or "dark" forms, there will almost certainly be provided an ample supply of thiamin—and incidentally other nutritional factors as well. It is doubtful, however, whether this criterion is reached in many American homes.

The solubility of thiamin in water results in considerable loss when fruits or vegetables containing it are soaked or cooked in large amounts of water which is afterwards discarded. Crushed fruits or vegetables lose more than those in which the cells are largely unbroken. Thiamin keeps well in the presence of acids, even when heated, but is destroyed by excessive or prolonged heating in the presence of alkalis like baking soda. It is a pity that so many cooks insist upon adding soda to water in which vegetables are cooked to help preserve their color, for in so doing they not only lose much valuable thiamin, but even larger amounts of vitamin C, which can often be still less afforded. In milk thiamin is particularly stable, possibly because it is accompanied by calcium, which somehow facilitates its utilization. It is not appreciably injured by ordinary boiling.

Tomato juice at its natural acidity, heated for an hour to the boiling point of water, loses only about 10 per cent of its thiamin and a moderate amount of vitamin C, whereas if it

is made slightly alkaline by addition of soda it loses 30 to 40 per cent of its thiamin and nearly all its vitamin C. In ordinary processes of cooking or canning of fruits and vegetables in which the juice is not discarded the thiamin content is fairly well preserved, quite in contrast to the severe destruction of vitamin C which occurs in many such products. The high temperatures required for canning vegetables and meats, however, result in a considerable destruction of their thiamin.

Although the inclusion of too much white bread in the diet only rarely leads to out-and-out beri-beri, it not infrequently leads to less obvious injury, such as loss of appetite, constipation, indigestion, weakness, and loss of weight. This is particularly likely to happen in American homes where white sugar, another refined food, has come to contribute much too large a proportion of the calories in the food. The average per capita consumption of sugar in America has increased nearly tenfold in the last hundred years. Since so much sugar is eaten, providing many calories but no vitamins, it is inevitable that some of the other foods will have to be particularly rich in thiamin, or else so much of them will have to be eaten in addition to the sugar that there will be an excess of calories and a consequent outbreak of bulging waistlines and double chins. The great American diet of steak, potatoes, white bread, and sugar is undoubtedly inadequate in thiamin unless the potato item and accessories are high in proportion to the sugar and bread.

There is still some uncertainty about the exact manner in which thiamin affects the body, and particularly the nerves, but one reason for its indispensability has definitely been pinned down to the fact that without it the metabolism of carbohydrates beyond the pyruvic acid stage (just before its final conversion into CO_2 and water) is interfered with,

and pyruvic acid accumulates, especially in the brain. It is doubtful whether carbohydrate metabolism can go forward in any living cell without thiamin. The most prevalent belief is that thiamin acts as an enzyme to bring about the final oxidation. It certainly enables isolated brain cells to do this. There is also some evidence that it enables the body to build fat out of the pyruvic acid. Just how the failure of the carbohydrate oxidation at the pyruvic acid stage interferes with the nervous system is still to be solved, but the speed of recovery when thiamin is injected under the skull of pigeons sitting with the back of the head touching the back, and turning cartwheels like a decapitated chicken, is little short of magical.

As would be expected, the more calories the body uses the more thiamin is required. This explains why the prodigious use of sweets by Americans, accompanied by extensive use of white bread, but with insufficient vegetables and whole grains, has plagued us with children who won't eat, and who become weak and sickly.

Only severe and continued lack of thiamin results in beriberi. The outstanding symptom of the disease is an extensive degeneration of the nervous system. Both motor and sensory nerves are affected, the former causing paralysis, the latter numbness, itching or prickling sensations, and painful sensitiveness to pressure. The nerve degenerations usually begin in the feet and legs and travel up. In many cases the skin and body cavities fill up with fluid, a condition called dropsy. The lungs, and also the cavity surrounding the heart, fill up with fluid, and the heart itself becomes enlarged and dilated, and slowed in its beat; usually death is caused by its sudden failure. Loss of appetite, constipation, languidness, breathlessness, muscular weakness and sensitiveness, and loss of voice are other characteristic symptoms.

The moaning whine of a baby with beri-beri is characteristic enough to afford a good diagnosis.

The nervous symptoms, dropsy, and severe heart troubles of typical beri-beri are seldom seen in Europe or America, and it was long thought that thiamin deficiency did not occur, but it is now believed that "subclinical" thiamin deficiency is extremely common in American infants and children, and also in women during pregnancy and while nursing. One of the first effects of insufficient thiamin is loss of appetite, probably brought about by an effect on the nerves of the digestive tract. There is less active secretion of digestive juices, less movement of stomach and intestine, slower emptying of the stomach, and greatly impaired absorption of the food that *is* digested. The relative immobility of the intestine is a common cause of gassiness and constipation also, whereas poor absorption may lead to diarrhea; sometimes one condition alternates with the other. People who have suffered from constipation for as long as fifteen years may have regular bowel movements after two months of treatment with thiamin. Children in institutions where the diet was thought to be adequate (300 units a day) have had their appetites improved so much when given 50 per cent extra thiamin that from 17 to 25 per cent more food was consumed. A dog with no interest in food in the morning may, after an injection of thiamin, devour his rations greedily in the evening.

Since most foods which contain thiamin also contain other vitamins, particularly those of the "B" family, it is not surprising that cases of pure thiamin deficiency are rare, and also that a great many people showing evidence of other vitamin deficiencies show some evidence of thiamin deficiency as well. Some degree of thiamin deficiency is undoubtedly a common and possibly an almost universal

accompaniment of pellagra and sprue, and it is undoubtedly involved as a complication in many diseases which affect the alimentary canal or liver. The neuritis and insomnia which frequently develop in dysentery, typhoid, typhus fever, malaria, metal poisoning, alcoholism, etc., is undoubtedly traceable to interference with the proper absorption and utilization of thiamin or other members of the "B" family.

Human requirements of thiamin vary with the weight and the number of calories consumed. For normal adults the amount required has generally been thought to be between 300 and 600 international units per day, or 1 to 2 milligrams, but some recent workers have reckoned it at twice this amount. Infants and growing children, whose calorie intake is relatively high, need more in proportion to their size. In some children it has been found that as high as 3.5 milligrams (1000 units) per day may be retained. There are a number of conditions in adult life also in which extra thiamin is needed, and in which a border-line diet may prove insufficient. People whose metabolism is accelerated by an over-enthusiastic thyroid gland, by pregnancy, or by such febrile diseases as malaria or typhoid, need more than normal individuals. Pregnant women very often develop symptoms of neuritis which indicate lack of sufficient thiamin, probably because of the heavy demands made by the fetus. Often the neuritis is accompanied by pernicious vomiting, low stomach acidity, and other gastro-intestinal troubles. It is difficult in this case to say which is the cart and which is the horse, but the vomiting and dyspepsia on the one hand and low thiamin on the other probably each aggravate the other, to the increasing distress of the patient.

Nursing mothers also require extra thiamin, for if they do not suffer themselves their offspring are liable to—as in the case of the people on the mandated Polynesian island

referred to above. Most mammals appear to be very inefficient in transferring thiamin to their milk; in order to supply their young with an adequate amount they need several times as much as normal or even pregnant animals do. About five or six times as much has to be fed to a rat mother to provide for the needs of her young as when the vitamin is fed directly to the pups.

Another group of individuals who are liable to suffer from deficiency of thiamin are the too-faithful devotees of John Barleycorn. Alcohol has long been blamed for producing a polyneuritis similar to that of beri-beri, but the alcohol is no more *directly* responsible for this than for injuries sustained in an automobile collision resulting from drunken driving.

The alcohol, like sugar, provides an abundance of calories with few vitamins. In addition, topers are notoriously neglectful concerning the non-alcoholic constituents of their diet. The result is a thiamin deficiency brought on by heightened demand and lowered intake. If alcoholics would supplement an otherwise adequate diet with about 0.125 mgs. (40 units) of thiamin per ounce of liquor consumed they would no longer suffer from the neuritis which is so distressing to many of them.

In its relation to carbohydrate metabolism thiamin is intimately related to insulin. In mild cases of diabetes a diet rich in thiamin over a long period will often improve and sometimes cure the condition. On the other hand, a scarcity of thiamin commonly leads to over-development of the islands of tissue in the pancreas which produce insulin. Insulin and thiamin seem to be partners in the business of managing carbohydrates in the body, and insufficiency of one may be made up to a limited extent by an overabundance of the other.

Although there is as yet no evidence that lack of thiamin causes it, the excruciatingly painful facial neuralgia known as "Tic douloureux" can usually be cured, at least temporarily, by injections of thiamin over a period of several months; sometimes liver extract, presumably to supply some other member of the "B" family, is needed as well. Instances are reported of elderly people with this disease being markedly improved after having suffered for over twenty years.

The most recent use found for thiamin is in connection with the treatment of syphilis of the nervous system. When syphilis has reached this stage the only effective drug is tryparsamide; this is dangerous to use because of injurious effects on the optic nerve, often leading to defects in vision or even blindness. Patients treated with thiamin for a few days before being given tryparsamide rarely suffer any injury to the eyes. If this is confirmed on a larger series of cases it may allow the use of tryparsamide in early syphilis and thus prevent neuro-syphilis from developing at all.

One other possible relationship of thiamin is in connection with virus diseases of the nervous system. In recent years nerve diseases such as poliomyelitis and encephalitis have become more prevalent than they used to be. Some people have seen in this a result of the terrific speed of modern life, the continuous round of hurry and worry, of jazz and jitterbugs, of cocktail parties and night-club life. But after all, our ancestors probably put in as much time worrying about witches and superstitions as we do about business and social prestige, and our predecessors who knew nothing of dictation and typewriters probably used up as much nervous energy, albeit more evenly distributed, as those of us who burn up the road getting to an office only to decorate the top of a desk with a pair of number eights while perusing the morning paper. It is at least worthy of some serious

thought whether a chronic mild deficiency of thiamin might not cause a sufficient interference with the normal health of our nervous systems to render them less resistant to virus infections.

When a deficiency of thiamin is discovered it is desirable to administer the vitamin in rather large doses until a normal condition is restored. A daily dose of 10 milligrams (3000 units) is considered conservative for abolishing an accumulated deficit. Even such a huge dose as 90 milligrams seems to be perfectly harmless. The neuritis disappears very rapidly unless the nervous system has been severely injured by a long-continued deficiency. The appetite returns as by magic, and the languor, weakness, and easy exhaustion are soon improved. Large doses of thiamin injected into the blood are a perfect sedative for cases of delirium tremens, and surpass any other treatment in obliterating writhing snakes and pink elephants from the minds of those who have been too long wedded to Ethyl Alcohol.

IV

THE OFFSPRING OF THE "B" FAMILY—RIBOFLAVINE, NICOTINIC ACID, ETC.

SOON after the wonderful effect of extracts of rice polishings on polyneuritis in pigeons and beri-beri in man was discovered, it was found that a water-soluble substance present in milk, yeast, and other foods was essential for growth in rats. At that time this was believed to be identical with the substance which would cure beri-beri. Rats deprived of foods containing it would in a few weeks lose weight, become weak and anemic, and die. One grain of compressed yeast would produce signs of returning health in a few hours, and there would be an immediate resumption of growth.

Experiments beginning about 1919 indicated that the substance which protected pigeons from polyneuritis and man from beri-beri was *not* identical with the substance that made it possible for rats to grow. Yeast could be heated to a point where its nerve-protecting powers were destroyed, and still be capable of promoting growth. Moreover, some substances, such as rice polishings and wheat germ, were found to be much more potent in protecting nerves than in promoting growth, whereas the opposite was true of such things as lean meat, egg white, and milk. The upshot of it was that after about seven years of argument and experiment the growth-promoting substance was recognized as a separate and distinct vitamin, and was christened B_2 in Europe and G in America, while the nerve-protecting sub-

stance was thenceforth known as B_1.[1]

About this time Dr. Goldberger and his associates of the United States Public Health Service discovered that vitamin G, or something associated with it in yeast, eggs, meat, etc., would cure pellagra. Pellagra is a first-rank scourge of the poorly nourished Southern share-croppers who dine the year around on little besides corn meal, salt pork, molasses, and coffee. A similar disease, called black-tongue, occurs in dogs, and it, too, was found to be cured by G-containing foods. Further complications developed when it was found that substances associated with vitamin G, but apparently not identical with the pellagra-preventing substance, protected rats and chicks from skin diseases. To make a long story short, it eventually developed that vitamin G as originally conceived was in reality a whole packet of vitamins, as full of separate entities as a roach's egg case; between 1928 and 1939 new vitamins and "factors" have been popping off from the vitamin G complex like fleas from a dead dog. The principal growth-promoting factor for rats, still sometimes called B_2 or G, turned out to be a yellow dye of a group called flavines; it has now been christened by the chemical name "riboflavine." The constituent which protects man from pellagra and dogs from black-tongue turned out to be an old familiar chemical, nicotinic acid, which Funk had found associated with vitamin B_1 in rice polishings twenty-seven years ago. The skin-protector for rats, called B_6 (part of what has been called vitamin H), has recently been obtained in pure crystalline form, and its chemical identity determined. It is probably also needed by human beings; injection of it into persons suffering from deficiency of the vitamin G complex, and manifesting great weakness,

[1] "F" and "G" were proposed for B_1 and B_2 in America, but "F" had already been tentatively assigned to a fatty acid found to be necessary for the nutrition of rats. Its use for B_1 would only have caused confusion.

brings almost immediate improvement. It has also been suggested that lack of it may predispose to chilblains. The skin-protector for chicks has turned out to be pantothenic acid and is probably universally needed by all living organisms. Various other factors supposed to be necessary for normal growth in birds or rats, or to prevent anemia, cataracts, gizzard lesions, failure of lactation, and even gray hair, have been described, but the distinctness of many of these is doubtful, and evidence of their need by human beings has yet to be obtained. For the present, at least, we need not concern ourselves about them as necessary parts of our daily diet.

RIBOFLAVINE

As noted above, when the principal growth-promoting member of the vitamin G family was finally unmasked, it proved to be a yellow dye of the flavine group which had long been known as a component of milk, egg white, meat, and many plant substances. Various names had been given to it according to its source, e.g., lactoflavine, ovoflavine, etc., but since these are apparently all alike, the name riboflavine, which has only chemical significance, has been approved for it. It is not easily destroyed either by heat or alkali. It forms combinations with phosphoric acid and proteins, and in the combined form acts as an enzyme which has an important function in the body in connection with oxidations. An interesting interrelation of vitamins appears from the fact that this "yellow enzyme" requires the assistance of a compound in which nicotinic acid, another of the vitamin B family, is an ingredient.

Young rats are unable to grow if deprived of riboflavine, and older animals rapidly lose weight and become unhealthy. Recently the failure of bone marrow cells to form

mature blood corpuscles in rats, associated with *one* of the vitamin G factors, appears to have been pinned to riboflavine, and there is a possibility of riboflavine scarcity being concerned with such conditions as "aplastic anemia" in man. A very remarkable fact about riboflavine in rats has been brought to light by the observations of Professor Szent-Györgyi that over a period of five years lousiness appeared exclusively in rats on riboflavine-deficient diets. When these lousy rats were fed riboflavine they promptly lost their lice, and diseased patches of skin developed new fur. This leads one to speculate as to whether Russian and Polish peasants lack sufficient riboflavine, and whether if it were rationed out to soldiers in war time it would help to control such louse-borne diseases as typhus and relapsing fever. Within the present year speculation as to this possibility has received support from an unsuspected angle. Experimenters at Harvard have found that lack of riboflavine renders rats highly susceptible to typhus.

We still have little accurate knowledge of the extent to which animals other than rats are dependent upon riboflavine in their food, but it is not likely that any higher animals can manufacture it. It is present in the flesh, liver, kidneys, and heart, and to a less extent in other organs of various animals, but whether some animals may be able to make their own or have it made by micro-organisms in their alimentary canals without importing it with the food is uncertain. Chicks are known to need it in the food, and recently it has been discovered that dogs provided with all known or suspected vitamins except riboflavine become yellow-livered and die. A dog in a state of utter collapse, apparently staring death in the face, can be returned to health within a few hours by injection of a few milligrams of riboflavine. It is likely, therefore, that the need for

riboflavine is quite general.

The principal visible symptom of lack of riboflavine in human beings is the development of lesions of the lips and mouth. Very characteristic are red, macerated transverse streaks at the corners of the mouth. This condition has been experimentally produced by diets lacking in riboflavine, and rapidly cured by its administration. Mouths showing these lesions are common in many parts of the tropics, especially in India, and are frequently seen in rural areas of our southern states where pellagra is also common, and where grits, biscuits, and a little home-cured pork are the principal items on the menu, to the exclusion of milk, cheese, eggs, fresh meat, or fresh vegetables. Five milligrams of riboflavine a day for three days was found to heal the mouths almost magically. Prior to an exact determination of what was lacking, children in India were cured by addition of skimmed milk or yeast to their diet of parboiled rice.

Riboflavine is widely distributed in plants, but grains and seeds are less richly endowed with it than with thiamin. Leaves and stems contain small amounts, especially the tops of beets, mustard, turnips, and carrots (for once spinach falls a *little* behind). Apricots and tomatoes are good sources, and also beef, veal, and chicken, but not fish or pork. Brewer's yeast is the richest vegetable source. Of ordinary human foods, milk, eggs, and liver are undoubtedly the best sources of riboflavine. Volume for volume, skimmed milk is richer in riboflavine than is cream, but since the latter contains nearly all the vitamin A, whole milk is usually preferable.

NICOTINIC ACID AND PELLAGRA

Pellagra, mal-de-rosa, or "sunburn of spring" as the Italians euphemistically call it, is a disease almost universally

associated with a diet in which white corn (maize) is the mainstay. One of the first theories about it was that it was a poisoning from spoiled corn. Then it was believed to be an infectious disease, either caused by a germ found in corn, or transmitted by insects in corn-growing regions. This idea was exploded by Dr. Goldberger, who demonstrated the immunity of well-fed people to the disease, even when exposed to it on all sides, and showed that such people failed to contract the disease from any sort of inoculations from pellagrins. There is no doubt, however, but that infectious diseases, especially of the alimentary canal, may be instrumental in precipitating a case of pellagra.

Pellagra is one of the modern curses of Egypt, and frequently breaks out, especially in spring, in many parts of Europe and Africa, but there is probably more pellagra at present in our own southern states than in any other place in the world. In the United States a total of over seven thousand deaths a year from pellagra is not an infrequent record. In some years there are more deaths from pellagra than from tuberculosis or malaria. The poverty-stricken share-croppers of the Mississippi valley, and negro laborers on cotton plantations throughout the southeast, have this disfiguring and disabling disease always with them. It rises and falls with the price of cotton, with the advent of local floods, droughts, and malaria epidemics, and with the rotation of the seasons, for all these factors are concerned in the ability of these people to add to their basic diet of corn, molasses, salt pork, and coffee. In the summer they usually piece out their meals with a few fresh greens, watermelons, and black-eyed peas, but in lean years the winter menu consists of corn for breakfast, maize for lunch, and hominy for supper, with an occasional catfish or swamp rabbit to break the everyday routine. Although many chil-

dren and adults of both sexes suffer from the disease, pregnant women and nursing mothers suffer most. In localities which are only mildly afflicted the disease appears year after year in the spring to disappear later, but each recurring attack in an individual seems to leave a permanent lowering of his resistance, both to this and to other diseases.

The disease begins with loss of weight and waning strength, together with vague grumbling complaints, poor appetite, and fretful disposition. Later burning sensations appear in the mouth, in which the mucous membrane becomes fiery red, swollen, and fissured, so that swallowing is an ordeal. The skin is marked by red, rough, scaly areas which burn and itch, and ultimately acquires the parchment-like texture of a mummy's skin. These red areas have a strange symmetry on the two sides of the body, and most commonly appear on the parts exposed to light—ugly, painful patches on the backs of the hands, on the tops of the feet, in necklace formations, and as "butterfly wings" on the cheeks. The digestive system is upset also; the mucous membrane, especially of the colon, becomes red, thick, and congested, and dyspepsia, diarrhea, nausea, and vomiting are common. There are nervous symptoms too—muscular cramps, tremors, and a characteristic mental condition of melancholia, lethargy, and stupor; in severe cases hallucinations and delirium make the sufferers quite irrational. The lesions of the nervous system are similar to those of beri-beri, but occur mainly in the central nervous system while those of beri-beri are more marked in the peripheral parts. Undoubtedly, however, nearly every case of pellagra is complicated by some degree of deficiency in vitamin B_1 as well. The majority of pellagrins have anemia to add to their burden of discomforts.

Alcoholics very often suffer from pellagra as well as

neuritis, and presumably for the same reason—lack of interest in non-alcoholic foods. There is a strong suspicion that sprue is another manifestation of the same deficiency as pellagra, complicated by infection with a yeast-like fungus; sore mouth, indigestion, diarrhea, and progressive anemia and wasting are the outstanding symptoms.

Years ago Dr. Goldberger observed that people who developed pellagra had poor diets, lacking particularly in fresh meat, eggs, and milk, and that if these and fresh vegetables were added to their bill of fare, pellagra could be prevented and cured. As noted above, the pellagra-preventing food factor was long ago known to be hidden somewhere in the vitamin G complex, but it was not until 1935 that it was clearly recognized as distinct from either riboflavine or B_6. Just two years ago (1937) the industrious group of nutrition workers at the University of Wisconsin, headed by Dr. Elvehjem, found that nicotinic acid would cure black-tongue in dogs. Since then it has been tried on human pellagra cases with dramatic success. Into the hospital of Duke University Medical School was brought a man who had suffered from pellagra for fifteen years, emaciated and dried up, covered with skin sores, mouth and tongue fiery red and swollen so he could barely swallow, mentally confused, diarrheic—a pretty thorough physical and mental wreck. He was given injections of 60 milligrams of nicotinic acid daily for eight days. His appearance was improved within twenty-four hours and his mind in forty-eight; in six days he had fully recovered his wits, and in twelve days his skin was normal—all by 10 cents' worth of nicotinic acid! To a Cincinnati hospital was brought an old skin-and-bone negress, mentally confused and semi-stuporous, unable to swallow or even to stand up, and expected to die. After three days of nicotinic acid treatment

her mouth became normal and she could eat. After a few weeks of building-up in the hospital she was discharged well enough to walk several miles to her home. Another case with badly inflamed mouth and vagina, skin sores, paralyzed legs, and scrambled mind, was dismissed a well woman in five weeks.

Nicotinic acid is an oxidation product of nicotine, but is about a thousand times less toxic. In the doses so far used in human treatments (60 milligrams a day by injection, or up to 1 gram a day by mouth), it produces no symptoms except a brief flushing and a little itching and tingling of the sore areas of skin and mucous membranes. Whether or not any nicotinic acid is obtained from smoking or chewing tobacco is doubtful. It is a substance found widely distributed in Nature in both plants and animals, and like thiamin is probably necessary to both.

Nicotinic acid is a durable substance, not destroyed by heat, ordinary acids, or alkalis, nor by exposure to air, so it is not likely to be injured by ordinary methods of food preparation. Most leaves contain it, but its distribution in grains and tubers is very irregular. It has recently been found that when rootlets are isolated from their parent plants and cultured in a nutrient solution of glucose and salts, they require traces of nicotinic acid as well as thiamin for continued growth. It has also been shown that cut tobacco leaves with their cut ends in a weak nicotinic acid solution absorb more water, live longer without wilting, and make much more nicotine than those in plain water. If this turns out to be generally true for cut stems and flowers, nicotinic acid may prove to be a boon to florists as well as to pellagrins.

The foods which have been found most effective in preventing or curing pellagra, and therefore presumably con-

tain most nicotinic acid, are red meat, fish, liver, eggs, peanuts, and most greens. Wheat germ is also well supplied, but oats and corn have practically none, and beans and peas very little. Milk is not a very good source, and for once the good old Irish potato also fails to come to the rescue. Dried brewer's yeast is the richest natural source, and since it contains *all* members of the B complex is particularly valuable both in prevention and treatment of pellagra. One ounce daily is usually adequate for treatment.

In the past, attempts have been made by the Public Health Service, Red Cross, and other Good Samaritan agencies, to relieve the suffering in pellagra outbreaks by supplying meat, fish, eggs, greens, and other good foods, but the expense has limited the accomplishments. Much good missionary work has been done in educating people in pellagrous areas to supplement their meager diets, if only with catfish, rabbits, and dandelion greens.

Now, however, the possibility looms of abolishing or at least alleviating pellagra wholesale by the simple expedient of adding a trace of nicotinic acid to the table salt, as for years we have been adding iodine in goiterous areas. The first large-scale use of nicotinic acid for the alleviation of human suffering was in 1938, when American scientists sent a large shipment of it to Spain to relieve 40,000 people suffering from pellagra in Madrid. It is hardly to be expected that pellagrins can often be made entirely well by the use of nicotinic acid alone, for the poor diet which deprived them of this vitamin is almost certain to have deprived them of others as well, particularly thiamin. Nevertheless, with the most severe deficiency rectified, the improvement in digestion and absorption may go far towards alleviating the other deficiencies. Meanwhile educational efforts can be directed towards the establishment of small vegetable

gardens, and the raising of more cows and chickens. Since enough nicotinic acid to cure the symptoms of uncomplicated pellagra can be obtained from a drugstore for little more than the cost of a dozen aspirin tablets, and it is harmless in ordinary doses, there seems to be ample justification for its widespread use in pellagra outbreaks. What this may eventually mean in prevention of human suffering and misery it is impossible yet to judge.

V

VITAMIN C

THE discovery and colonization of America by dauntless explorers from Europe in the fifteenth and sixteenth centuries did not result in the anticipated inflow of spices and pearls, but it did result in the introduction of other things into Europe, some of which have had very profound effects, though most books of history, more concerned with politics and war than with health and happiness, seldom mention them. Tobacco, corn, potatoes, and very likely syphilis, are some of the outstanding importations for which Europe can thank—or else curse—America. Of the items in this list, the potato is a blessing which has been of more permanent benefit to Europe than even our war loans or the spendings of our tourists. Before the potato—for which the Irish deserve no credit, except for their appreciation of it—was introduced into Europe, scurvy was as common throughout the northern part of that continent as beriberi was in the Orient, and a large proportion of the poorer classes suffered from it in some degree every winter. The "spring fever" of the European peasant was not an exuberance of youthful whims and fancies as now known to us, but was a miserable condition of lethargy, gloom, and irritability, of swollen gums and aching legs, which led the unfortunate sufferers to search for and nibble at the first sprouts and greens to follow the melting snows. Nowadays scurvy is rarely seen in Europe except when there is a failure of the potato crop, as in 1917.

The prevalence of mild scurvy in European peasants has often been overlooked, due to the far greater suffering and untold misery which almost invariably accompanied long sea voyages, military expeditions, or explorations. Scurvy has rightly been called "the plague of the sea and the spoyle of mariners." When Vasco da Gama made his epochal trip around the Cape of Good Hope in 1498, scurvy carried off 100 of his 160 men. There is a record of a Spanish galleon being found adrift at sea with the entire crew dead of this disease.

When Cartier made his second journey to Newfoundland in 1536, he wintered near an Indian Village in Quebec. Of 103 men, 100 were desperately ill with scurvy and 25 died, and this in spite of the most pious prayers and supplications to the Lord. The Indians also suffered. One Indian, however, who had been ill ten or twelve days earlier, was found running about in a state of amazing good health. It developed that he had been browsing on the leaves of a local tree (believed to be a spruce). A decoction was made from these leaves and fed to Cartier's crew. The narrator says of the results: "It wrought so well that if all the physicians of Montpelier and Lausanne had been there with all the drugs of Alexandria they would not have done as much in one year as that tree did in six days, for it did so prevaile that as many as used it by the grace of God recovered their health." The narrator was undoubtedly quite right about the physicians and their drugs, for in that day the juice of citrus fruits was not among the drugs even of Alexandria. In 1734, a ship in the Arctic Sea had on board a man so disabled by scurvy that there was no hope of his recovery and he was set ashore in Greenland with his gums swollen and bleeding, his teeth falling out, his skin dotted with subcutaneous hemorrhages, and his legs so painful

and paralyzed that he was unable to stand. He fed upon a local grass which he plucked with his teeth—and made a perfect recovery.

Vitamin C has been shown to be a carbohydrate acid, for which the name ascorbic acid has been approved. The presence of this substance in fresh fruits was discovered before it was known to have anything to do with the prevention of scurvy, and its presence was put to practical use in distinguishing between fresh and stale fruits, and between natural and artificial fruit juices. It can now be prepared synthetically, and can be tested for by chemical tests delicate enough to detect it in a fraction of a drop of orange juice.

Ascorbic acid is very widely distributed in Nature. Like vitamin B_1 it is concerned with respiration, and is needed by active tissues of both plants and animals. It is found in greatest abundance in the busiest tissues. In plants it is abundant in green parts, especially where there is active growth, and also in fruits and tubers where rapid growth and storage of food materials is taking place, but unlike thiamin it is not stored in seeds or nuts. Thiamin stored in the seeds is all that is necessary to start the process of growth; as soon as germination begins, the young growing plants immediately begin manufacturing ascorbic acid. Any kind of seeds soaked in water for twenty-four hours and then kept in a moist place for a few days till they sprout will become enriched with it. In times of famine when grains, beans, peas, or other seeds might be more readily obtained than fresh vegetables, sprouting these would afford a valuable source of this indispensable vitamin.

In animals the largest amounts of ascorbic acid are found in such active organs as the adrenal glands, liver, brain, etc., and in only small amounts in the muscle meat. Eggs contain practically none, although the developing chicks begin pro-

ducing it as soon as they start their growth. Milk of animals such as cows, which manufacture their own ascorbic acid, contains moderate amounts of this vitamin, even if no fresh fodder containing it is obtained by the animals, but milk of human beings, apes, and guinea pigs, which seem to be the only animals incapable of synthesizing their own vitamin C, varies with the diet. A well-fed human mother has four or five times as much ascorbic acid in her milk as has a well-fed cow, but when she is on a diet deficient in this vitamin, her milk may be almost entirely devoid of it.

One of the richest sources of ascorbic acid is the juice of citrus fruits, especially oranges, lemons, and grapefruit. Next come greens and green vegetables, and then fresh fruits, onions, and potatoes.

There are other points to consider in studying sources of ascorbic acid than the amount of it contained in an ounce of unprepared food. Horse-radish and red peppers have about ten times as much per ounce as have potatoes, yet potatoes are of far greater importance to the human race as a source of vitamins. Fresh green peas, fresh cucumbers, and fresh strawberries are all richer sources of ascorbic acid, ounce for ounce, than are apples or potatoes, but when winter comes the canned peas, strawberry jam, and cucumber pickles are no longer even fair sources of the vitamin, whereas the apples and potatoes stored in the basement, even when boiled, baked, or made into pie, still contain important amounts of it.

Ascorbic acid is a very delicate substance, and must be handled with care. Its outstanding peculiarity is its sensitiveness to oxygen, and when oxidized, other than by a delicate reversible method occurring in the body, it becomes worthless. Heat, and even light, speeds up the process of oxidation, which explains why cooking with exposure to air

is very destructive to it. Even at ordinary room temperatures the vitamin is quickly destroyed in milk, vegetables, etc., exposed to the air, although it is well preserved in bananas, apples, potatoes, etc., in which it is protected by the enclosing skin. Spinach exposed on a market table, even if kept moist and unwilted, loses about half its ascorbic acid in three days and practically all of it in a week, whereas in a refrigerator it hardly deteriorates at all.

Many vegetables and fruits contain an enzyme which, when liberated from the plant cells, greatly hastens the destruction of ascorbic acid. This is why such raw vegetables as spinach, cabbage, turnips, carrots, etc., lose their vitamin very quickly after being crushed, grated, or shredded; they should never be so treated until just before serving, or just before immersion in hot water to kill the enzyme. It is because of the presence of this enzyme that many raw vegetable and fruit juices are practically devoid of the vitamin, whereas others retain it very well. Cider is ordinarily almost entirely lacking in it, even if pressed from apples well supplied with it, whereas orange and tomato juice lose it very slowly.

The loss of vitamin C is accelerated when soda is added to fruits or vegetables when they are cooked, for the vitamin seems to be preserved best at the natural acidity of the substance in which it is found. The housewife's trick of keeping vegetables green or of neutralizing the acidity of tomatoes by adding soda to the cooking water is an invention of the devil, for it greatly hastens the loss of both ascorbic acid and thiamin. Most of us can ill afford such a reckless waste. Another important point is to avoid any copper or copper alloys in cooking vessels or utensils. Even such small amounts of copper as a chemist would have difficulty in detecting may be sufficient to cause almost complete loss of as-

corbic acid during cooking. It is probable that fruits or vegetables sprayed with copper compounds, such as Bordeaux mixture, would lose nearly all of this vitamin when cooked unless very thoroughly washed beforehand.

Still other factors influence the richness of foods in ascorbic acid. Different varieties of apples, potatoes, tomatoes, etc., may vary within several hundred per cent in their ascorbic acid content, and they also vary with their ripeness, the season of the year, and the nature of the soil in which they are grown. Apples, for instance, vary from 0.5 to 3.5 milligrams per ounce; McIntoshes and Delicious are at the lower end of the scale, while Baldwins, Winesaps, and Newtons rank high. In view of the fact that in our northern states apples constitute an important source of ascorbic acid during the winter, it is evident that more attention should be paid to this factor in the development of orchards and the marketing of apples. In all kinds of apples a large part of the vitamin is found in the peelings, so it is fortunate that few people have the obnoxious habit of peeling apples before eating them. Packers of tomatoes and tomato juice should consider the vitamin content of the varieties they use, and distribute only the seeds of varieties rich in vitamins to the farmers who supply the canneries. Soil conditions are also important. Spinach grown on uplands is 50 per cent richer in ascorbic acid than that grown in mucky soil, and fall spinach is richer than summer spinach. Tomatoes, peppers, and fruits increase their ascorbic acid as they ripen, while greens, corn, peas, and snap beans are richest during the period of rapid growth, while still in the tender stage.

Few animal products are important sources of ascorbic acid. Cooked muscle meat contains almost none, although such organs as liver, sweetbreads, brain, etc., may contribute some. In spite of this the great arctic explorer Stefansson

and his friend Anderson proved that not only Eskimos and explorers in the arctic regions, but the same explorers in New York, could live on nothing but meat and fat with no signs of vitamin C deficiency. Possibly fresh meat will be found to contain something that a human being, but not a guinea pig, can convert into ascorbic acid. It is probable that there are varying degrees of efficiency in the manufacture of ascorbic acid in different animals, and man may not be as helpless as guinea pigs. No one has yet found out exactly from what substances animals like rats and cattle make their ascorbic acid, although recently it has been discovered that rats make use of some constituent of certain fats.

Eggs and dairy products, other than fresh milk, are useless as sources of this vitamin. Human milk normally has much larger amounts of ascorbic acid than cow's milk, but varies greatly with the diet. Cow's milk is not a reliable source, and pasteurization destroys a large part of the vitamin C present. Since the advantages of pasteurization of milk far overshadow the disadvantage from loss of an amount of the vitamin, which was not of great importance in the first place, it is the course of wisdom not to rely on milk for this vitamin at all, but to fortify the diet, especially of infants, with orange or tomato juice.

The result of severe and continued deficiency in vitamin C is scurvy, and it was once thought that the vitamin C requirements were taken care of if enough was eaten to prevent this disease. Actually, ascorbic acid plays several important rôles in the body, and scurvy is a late symptom premonitory of death. Its absence is no more a true measure of adequate ascorbic acid than absence of cretinism is a measure of adequate thyroid secretion, or absence of starvation a measure of an adequate economic condition. It was many years after mariners and explorers were saved from scorbutic deaths by

the use of citrus fruits before babies were similarly protected. There was too much emphasis on sterilization and calories, and not enough on vitamins. Pale, fretful, irritable babies with worried expressions, who are in evident pain when they move and cry out when handled, are very likely the victims of a diet of boiled milk and gruel, almost entirely lacking in ascorbic acid. If they have teeth they will also have painful, swollen, bleeding gums. Scurvy in adults is seldom seen any more. It was characterized by painful, aching joints, easily fractured bones, swollen, bleeding gums, a body spotted with burst skin capillaries, a pallid, dirty complexion, a condition of weakness, lethargy, and weariness, and a mind clouded by gloom and inordinate cantankerousness.

In mild vitamin C deficiencies there may be no other symptoms than a tired feeling, a tendency to rheumatic aches, easily broken capillaries, anemia, and a mental apathy and irritability. Ascorbic acid is a magic potion for increasing the joy of living. Some philosopher once aptly remarked how unfortunate it was that so much youth is wasted on the very young. In ascorbic acid we have a precious substance which preserves some of this fleeting youth for later years when it can be more fully appreciated and more advantageously utilized. Since vitamin C deficiency rarely occurs uncontaminated by other deficiencies, it is not always easy to say just how much of the "below-parness" is due to this deficiency.

One of the rôles of ascorbic acid in the body is to help in oxidation processes by acting as a go-between for hydrogen. It plucks hydrogen from one molecule and transfers it to another, and keeps repeating this process over and over. Its function may be compared roughly to that of a truck which carries load after load of sawdust from a lumber mill

to a dumping ground, and thus keeps the mill from burying itself in its own wastes. There are several other substances in the body which perform similar functions in connection with oxidations, and it is possible that to a limited extent this function may be taken over by these other substances when ascorbic acid is not present to the saturation point.

Another important rôle of ascorbic acid is to cause the "ground substance" between the cells of connective and supporting tissues to "set" or "jell." Without ascorbic acid this ground substance remains fluid and lacks "substance" in places where it should be gelatinous or gristly, or where it should be hardened by deposits of lime and phosphorus to form bone, dentine, or enamel. In bones the bone-forming cells first relapse into ordinary connective tissue cells which produce fibrous and gelatinous substances instead of true bone, causing the bones to become weak and easily fractured, and the joints to become enlarged and painful. In severe deficiencies even the fibre and gelatine fail to form. In the teeth a mild deficiency causes the laying down of a defective bone-like material instead of the dense, hard dentine and enamel, and in more severe deficiency the teeth become porous, deformed, and loosened from their sockets. Saturation of the body with ascorbic acid may also protect teeth against decay by assisting in the development of immunity against acidophilus bacilli.

The lens of the eye contains much ascorbic acid, and lack of it is one of the factors concerned in the development of cataracts.

One of the earliest and in all stages the most striking effects of ascorbic acid is on the capillaries. When there is inadequate ascorbic acid, the delicate cells which form the walls of the capillaries are still able to multiply, but no new capillaries form, apparently because the cells fail to form a

cementing substance to bind them together. They are as insubstantial as a wall of bricks without mortar. The existing capillaries become so fragile that they are broken under the slightest strain, and allow blood to ooze out into the surrounding tissue. This may result in anything from pin-head spots to severe hemorrhages, and they may occur in the skin, stomach, intestine, kidneys, or other internal organs. The fragile capillaries are particularly liable to break where there is rubbing, straining, or pressure—where the diaper rubs on babies, where the skin stretches over joints or around teeth in the gums, or where there are bumps or bruises. Nosebleed is common, and there is often blood in the feces and urine.

Another important function of ascorbic acid seems to be the neutralization of various poisons in the body, particularly some produced by infections. It is distinctly protective in such diseases as diphtheria, tuberculosis, infantile paralysis, whooping cough, and rheumatic fever. A recent investigation showed that certain types of disease germs were found five times as frequently in the tonsils of children whose blood was low in ascorbic acid as in children who were well supplied, but in this case it is hard to decide which is the cart and which is the horse. Ascorbic acid is used up in much greater quantities in the presence of certain diseases, and it is just as likely that the tonsil infection depleted the blood of the vitamin as that a low level of the vitamin allowed the germs to get a foothold. Heightened temperature itself greatly increases the amount of ascorbic acid used up, as shown by artificially induced "hot box" fever. The importance of abundant ascorbic acid when the body is ravaged by disease is obvious. It has recently been shown to be the ideal sedative for insomnia resulting from exhaustion of nerves by toxic products of disease.

It has also been observed that ascorbic acid hastens the healing of wounds. It probably does this in at least three different ways—by aiding in the formation of new capillaries, by allowing the formation of fibrous connective tissue, and by neutralizing toxic substances produced by infection. There is even some suspicion that ascorbic acid may be necessary for the formation of new blood cells; at least it has a regulatory function in this connection. This would account for the pallor that is so characteristic of scurvy.

Ascorbic acid also has an important relation to the "complement" of the blood, an enzyme-like substance concerned with immunity. The complement rises and falls with the ascorbic acid, and it is quite possible that the vitamin enters into its composition. Even more important is the demonstration that ascorbic acid stimulates the development of antibodies, by means of which animals react against infections and other invasions of their tissues.

The most recently discovered function of ascorbic acid is that of a protection and a cure for chronic lead poisoning. Lead combines with ascorbic acid in the body so avidly that early symptoms of scurvy may appear in cases of lead poisoning even on a diet which contains considerable amounts of the vitamin. The body apparently suffers partly from lead poisoning and partly from scurvy. If, however, a generous excess of ascorbic acid is provided, the lead is practically all handcuffed to the vitamin and deported with the feces, and an adequate amount of the vitamin is left over for normal use in the body. Evidences of lead poisoning were common among house painters at Oberlin, but four of the painters had unknowingly protected themselves for years by eating a diet unusually rich in ascorbic acid.

Ideas about the amount of ascorbic acid which we need for perfect health have undergone considerable change. Re-

cent dye methods have made it possible to measure the amounts of ascorbic acid in blood, tissues, urine, etc., as well as in foods, so easily that its use in the body, its excretion, etc., can be studied almost as easily as that of sugar. Tests for capillary fragility are now performed to detect actually inadequate amounts of the vitamin, but it is possible that best health is maintained when the daily ascorbic acid intake is considerably greater, so that the tissues are saturated with it. Under these conditions about a third of the amount eaten is excreted in the urine, but if the saturation point is passed, practically all of the excess is excreted. It has not been proved that it is necessary to maintain this saturated state, but it certainly does no harm, and it provides a good margin of safety in emergencies. Unusually large amounts are needed by the body not only in the presence of various infectious diseases and other types of poisoning, but also when the rate of living is speeded up by an over-active thyroid, fever, high protein diet, or other causes. Sometimes, also, unusually large amounts are lost, especially when we do some good serious sweating. The Bantu laborers in South African gold mines, for instance, may lose as much as five pounds in weight during an eight-hour shift underground, most of it in sweat. The sweat contains so much ascorbic acid that at this rate they lose about 2 milligrams per hour in *addition* to the normal loss in the urine. Children, and especially babies, who have a higher rate of metabolism than adults, need more ascorbic acid in proportion to their weight than do their elders.

The most recent estimates of the daily amount of ascorbic acid needed for perfect health, and with a good margin of safety, lies between 30 and 60 milligrams for adults, and about half that for babies, with intermediate amounts for children, depending upon their age and activity. Some

writers set barely adequate amounts at about 20 or even 40 milligrams for babies, 40 for children, and 50 or 60 for adults, but the apparent good health of large groups of people who do not get this much makes it doubtful whether an intake of ascorbic acid to the saturation point is really needed, except possibly for expectant and nursing mothers. Recent estimates for pregnant women run as high as 75-125 mg., and for nursing women 100 to 150 mg. (=5 to 8 oz. of orange juice) per day.

An idea of the food necessary to provide us with our daily ascorbic acid can be obtained from the following table of approximate milligrams per ounce (milk per pint):

Citrus fruit juice	18-20 mg.
Tomatoes or tomato juice	8-10 mg.
Greens properly cooked	5-10 mg.
Raw green peppers	50 mg.
Fresh raw vegetables	5-10 mg.
Cooked fresh or canned vegetables	2-5 mg.
Potatoes, properly cooked	3-5 mg.
Pineapple and strawberries, fresh	8 mg.
Pineapple, canned or juice	3 mg.
Apples and most other fruits	0.5-3.5 mg.
Pasteurized milk, per pint	3-6 mg.

All the abnormal conditions of bones, teeth, joints, capillaries, and disposition due to lack of ascorbic acid are improved within a few hours after the vitamin is provided. Scurvy responds to it as magically as neuritis does to thiamin, or pellagra to nicotinic acid. Pure ascorbic acid is now available in crystalline or tablet form, but it must not be dissolved until immediately before use or it will deteriorate. Apparently no harmful effects result from the continued use of large doses, even up to 500 milligrams per day. When

the ascorbic acid reaches a certain concentration in the blood, the kidneys eliminate it, apparently without the least difficulty. The capillaries show improved resistance to breaking within a few hours after a dose of ascorbic acid, and very sick babies show remarkable improvement in one or two days. The bone and tooth injuries take longer to repair, and in severe scurvy overdoses of the vitamin should be provided for several weeks.

VI

VITAMIN D, THE SUNSHINE VITAMIN, AND OTHER FAT-SOLUBLE VITAMINS

ALTHOUGH the human race began to suffer from vitamin A deficiency soon after it learned to cultivate and store grain and to live upon it too exclusively during unproductive seasons or in lean years, widespread injury from insufficient vitamin D came much later. It became a major human scourge when the development of industrialism and the growth of great cities in the northern part of Europe deprived mankind of sufficient sunshine. This is because exposure to sunshine is necessary for the formation of vitamin D in our own skins from a mother substance which seems always to be present in abundance.

The combination of window glass, smoke, slums, and malnutrition which arose during the sixteenth and seventeenth centuries in Europe was too much, even for our stalwart forefathers, in a locality in which sunshine was already diluted almost to the vanishing point by fog and latitude. From that time until the beginning of our present century, rickets, which comes from lack of vitamin D, was the commonest disease of children under two years of age. Children with extreme deformities were very common. Everywhere there were to be seen bowlegs, knock-knees, deformed wrists and ankles, protruding foreheads, potbellies, and "rosaries" along the sides of the chest. Most of the children later outgrew these troubles, but not all, and a roving eye on a modern bathing beach can still pick out a fair number of

middle-aged people, who were babies some forty years ago, whose legs would spell "OX" if they stood together in properly assorted pairs.

In the northern European cities, and in our own, from 80 to 90 per cent of the babies formerly showed some evidence of rickets. Very few babies in Boston or New York, especially those born in winter, escaped it, and among the black babies of Harlem and the dark "bambinos" of the East Side one could have searched in vain for an example of what the well-fed baby should look like. In a survey made in New Haven about 1925, 96 per cent of children examined by X-ray showed evidence of rickets at some time before they were eight months old, even though over half of them were given preventive or curative treatment. Even in New Orleans rickets in milder form was very prevalent, for there are many cloudy murky days, and when the sun does shine, at least in summer, it does it with such reckless abandon that mothers take siestas in darkened bedrooms, children play in cellars, and babies are perambulated in the moonshine.

Today, with sunbaths and ultraviolet lamps among our most popular health hobbies, and cod-liver oil or other rich sources of vitamin D almost as much a matter of routine in the raising of a baby as castor oil or orange juice, the day of obvious rickets has gone the way of witchcraft and louse-repelling sachets, and it is only seen in the most benighted parts of the civilized world. *Early* symptoms of vitamin D deficiency are still very common in infants and "overbearing" but underfed mothers in the North Temperate Zone, but they are not often, nowadays, severe enough to leave indelible marks.

Vitamin D is a fat-soluble substance like vitamin A. It was many years before the two were separated from each other, for most foods which supply vitamin D supply some

vitamin A also. Then it was found that cod-liver oil in which all vitamin A had been destroyed was still able to prevent rickets. Vitamin D went through the process of being born into the scientific world in 1921 and 1922, and was christened in 1923.

Vitamin D is formed by the action of ultraviolet light rays on certain wax-like substances, related to fats, which are known as "sterols." Cholesterol, very abundant in animal bodies, is one of these sterols, but pure cholesterol is not one of those which light can change into vitamin D. However, it is accompanied by a related substance, possibly derived from it, which *is* changed into vitamin D when bombarded by ultraviolet rays. When the skin is exposed to sunlight the production of vitamin D from this hanger-on of cholesterol takes place. An identical form of vitamin D is found in the livers of fishes, along with certain other forms. Another sterol, called ergosterol, which is changed into a different vitamin D by the action of light, is found abundantly in yeasts and various fungi. A still different form of vitamin D results from the irradiation of higher plants. Altogether eleven different varieties of vitamin D are known.

The only place in Nature where vitamin D is found abundantly under conditions which do not suggest its formation from mother substances by the action of ultraviolet light is in the oil of fat-livered fishes. There is good reason to believe that these fish actually manufacture vitamin D in their livers without the aid of light, for they live in northern waters where ultraviolet light must be as scarce as in a New York tenement house in winter, and they feed on smaller organisms that likewise live where they would never need to worry about getting sunburned. One other explanation that has been offered for this mystery is that seaweeds or plank-

ton in the clear sunlit waters of the Caribbean might be the original source. Vitamin D has actually been found in oil extracted from Sargassum weed. Enormous quantities of the weed are carried northward by the Gulf Stream; meanwhile its vitamin D is taken up by countless tiny marine molluscs and crustaceans which feed on it. These pass the vitamin on to shrimp and sardines, and these in turn yield it up to the large tunas and cod which migrate with their drifting food factories. Thus eventually the vitamin D finds its way to the great human fish centers of Europe and America, and thence as cod-liver oil to the shelves of drugstores in every town and hamlet in the world. Against this idea, however, is the fact that when pure flavorless vitamin D is distilled from the livers of various fish by the recently devised vacuum distillation process, different kinds of fish are found to have their livers charged with different brands of vitamin D. The tuna fish brand, for instance, is different from the sea-bass brand, and even cod-liver oil contains two major varieties and several minor ones.

Unfortunately the livers of land animals are unable to function like those of fishes. This results in an important difference between the mother substances of vitamin A and those of vitamin D, for while carotene is as useful a food as vitamin A because it can always be converted into vitamin A in our own bodies, the forerunners of vitamin D cannot be so changed except on exposure to ultraviolet rays.

Very few natural foods contain appreciable amounts of vitamin D. Milk, butter, eggs, liver, and fat-fleshed fish practically complete the list. The oil of fat-livered fishes is the most potent natural source, and it is from this and from irradiated yeast that we obtain our concentrated forms of vitamin D. Pure "calciferol," the most potent product of irradiated ergosterol, is 400,000 times as potent as cod-liver

oil. Yet to equal a teaspoonful of standard cod-liver oil it takes about eight quarts of summer milk from sunbathed cows, sixty quarts of winter milk, twelve to sixteen ounces of butter, two pounds of liver, five eggs from outdoor hens in summer, or about a dozen winter eggs. Human milk is never very rich in vitamin D, even when mothers dutifully take cod-liver oil to supply it. Moderate exposure of the body to summer sunshine or to rays from a mercury vapor lamp is in most individuals an adequate substitute for *any* vitamin D in the food. Nevertheless, giving babies cod-liver oil or vitamin D concentrates of some kind is usually far less troublesome than irradiating them.

Vitamin D may also be supplied to human beings by being added to foods, or formed in them by irradiation. These methods have been most extensively and effectively applied to milk. The vitamin D content of milk may be increased by any one of three methods: direct addition of it (fortified milk); feeding of irradiated yeast to the producing cows (metabolized milk); or irradiating the milk itself, in which case enough provitamin D is activated to provide a minimum of about 135 units per quart.

The effectiveness of sunlight as a means of forming vitamin D in our own skins depends upon its content of the particular ultraviolet light rays needed. The effective light rays are largely filtered out by the earth's atmosphere, especially when this is full of fog, smoke, or dust, or when the light has to travel through a much thicker layer due to a low position of the sun above the horizon. It is for this reason that sunlight, even if there is any, is largely or completely robbed of the effective ultraviolet rays in the far north, in most of Europe and North America in winter, and in foggy cities like Glasgow and London, or smoky cities like St. Louis and Pittsburgh almost any time. On the other hand, in the

tropics, at high altitudes or on sunny beaches, if the sun is taken advantage of, cod-liver oil is as needless as is rain on the ocean. Water, and snow even more, reflect the ultraviolet rays and so increase their availability, as every parboiled bather and mountain climber knows. When the sunlight contains plenty of the desired rays, even the "skyshine" of shaded places is effective, since these rays are well reflected. Ordinary window glass completely bars them out.

Animals obtain most of their vitamin D by their grooming operations. A cat licking her fur is getting her daily vitamin D as well as taking a bath. Wool fat and skin oils in general are rich in provitamin which is changed to vitamin D on exposure to light. If animals are not allowed to lick their fur they get no benefit from sunlight. Carnivorous animals get vitamin D from the fur and feathers of their prey. Birds anoint their feathers with a provitamin D provided by the oil gland. Since birds have no glands in their skins except this one, they suffer from rickets when it is removed, in spite of exposure to sun.

It will be welcome news to small boys that too frequent washing of human skin, especially with soap, is an unhygienic procedure, for it removes too much of the sebaceous skin secretion out of which sunshine produces vitamin D. Too great addiction to bathing may necessitate the use of cod-liver oil even in the tropics. It is evident that Nature did not intend human beings to be semi-aquatic.

It seems from these facts that a good deal of the vitamin D formed in human skin is really formed *on* it and then reabsorbed. It is possible to cure rickets in rats by applying vitamin D preparations to the surface of the skin, but it takes about ten times as much as when it is given by mouth. This seems to be a good argument against using it as a "skin food" instead of eating it. However, in cases of obstructive

jaundice, application to the skin might be desirable, for vitamin D, like vitamin A, is not absorbed from the intestine in the absence of bile.

The mode of action of vitamin D is rather complicated because it is only one of several factors concerned in its sphere of influence. It has a specific effect on the absorption, retention, and distribution of two minerals in the body—calcium and phosphorus. Both are absolutely essential to life, from the moment of conception to death. They are intimately concerned with the never-ceasing metabolism of every living cell in the body. But in addition bones and teeth are made of a combination of these two elements. Nature loves to kill two birds with one stone, and does it every time an opportunity offers. Just as she makes use of stored fat as an insulator and shock absorber, so she makes use of stored calcium and phosphorus as the props and barrel staves of the skeleton. In both cases the more vital functions come first, and if there is a scarcity the inactive stores, however helpful they may be in a mechanical or physical way, have to depend on what is left over, or go without. And if the scarcity becomes more acute the inactive stores are actually melted down and used, just as gold ornaments might have been melted down and used for currency in times of stress.

When calcium or phosphorus or both become scarce in the body, the normal process of bone formation ceases. Normally during bone growth the cartilage which precedes the bone (all long bones have growing cartilaginous regions near their tips) is eroded away and bone cells come in, depositing calcium phosphate as they multiply. When there is a deficiency of either one or both minerals, no calcium phosphate is formed and the cartilage is not eroded away, but bone cells accumulate just the same. The consequence is that the bones remain soft and weak, bend under pressure, and

enlarge at the joints. Hence the bowlegs, square heads, knock knees, pigeon breast, deformed pelvis, bulging ankles, and the row of bead-like enlargements where bone and cartilage join on the ribs, so aptly called the rhachitic rosary.

Teething and walking are delayed. Both the dentine and the enamel of the teeth are imperfectly deposited, and the teeth become soft and porous, and susceptible to decay. A recent survey of 1,400,000 American children showed that in the northern states 76 per cent had cavities in their permanent teeth, with an average of 293 cavities per 100 children, while in the South only 60 per cent had cavities, with an average of 202 per 100 children. It is probable that sunshine had more to do with it than either diet or table manners. As noted before, many of the defects of vitamin D deficiency are later corrected, but the deformities of teeth and pelvis are liable to persist. The latter may cause much grief later in life when child-bearing begins.

Exactly how vitamin D keeps the calcium and phosphorus regulated and functioning properly is not fully known. It undoubtedly makes the absorption of minerals more efficient, and impedes their excretion, but it is also concerned with the form they take and the distribution of them inside the body. For example, vitamin D probably increases the phosphorus in the blood to a point where it is properly balanced with the calcium for bone forming, by releasing it from lecithin or other organic combinations. If the minerals in the diet are badly off balance when rapid growth is occurring, there is a heavy demand for vitamin D.

It is most often in babies from six to eighteen months old that rickets develops. It rarely develops before birth due to the efficiency of the placenta in taking minerals from the mother, combined with the wise and merciful provision of Nature which keeps babies flexible by postponing the exten-

sive storage of calcium and phosphorus in the bones until after birth. When the infantile period of very rapid bone growth slows up, outdoor life begins and more varied food is eaten. Increased minerals, sunshine, and vitamin D in the food, any one or all, not only stop the disease but usually cure it.

The same conditions which lead to rickets in infants sometimes, but much less frequently, lead to a disease called osteomalacia, or softening of the bones, in adults. Immediately following the World War there developed in Vienna and other Central European cities a condition of weakened legs, painful bones, waddling gait, and posterior lap (due to abnormal spine curvature), which was called marmalade legs in tribute to one of the outstanding features of the much restricted diet. The widespread misery of those dark days came while help was close at hand—it never would have happened if the brilliant discoveries concerning the value of ultraviolet rays and vitamin D had come a few years sooner. Oddly it was almost entirely confined to men.

In almost every other known instance osteomalacia is primarily, and almost exclusively, a disease of women. Presumably the hormones from the ovary are somehow involved in it, for it usually develops at times when the reproductive system is especially active—at puberty, during pregnancy, and while nursing. It develops especially in mothers who do more than their share towards keeping up the quantity if not the quality of the human race.

It was formerly thought that it was the drain of minerals by the fetus or nursing baby that caused this condition, but the fact that it very commonly develops just at puberty, and during the early part of pregnancy when no baby bones are yet being formed, points to the ovaries as the disturbing factor. As much as two-thirds of the minerals in the bones

may be melted away, and the softening of the skeleton may go so far as to make walking or even standing impossible. The pelvis is especially likely to be deformed so that natural births become difficult or impossible. Wherever Caesarean sections are unduly prevalent there is probably need for sunlight, minerals, or vitamin D, one or all. Severe lack or wasting of calcium also causes tetany, in which the muscles twitch and convulsively contract. This is due to an overexcitable state of the nerves which always follows insufficient calcium in the blood.

In addition to its principal business of regulating the behavior of the calcium and phosphorus in the body, vitamin D undoubtedly has other minor functions. It stimulates metabolism, as does the thyroid gland; hedgehogs given it fail to go to sleep for the winter. Because of its effect on phosphorus it is important in connection with numerous other affairs of the body with which this element is concerned. Vitamin D may also prove to be a godsend to adolescents, for recently it has been found to give excellent results in the treatment of acne and other skin conditions, and few things are more mortifying than acne to sub-debs or their suitors. There is, however, little justification for taking this or any other vitamin externally in cosmetics instead of internally.

Usually both rickets and osteomalacia go hand in hand with poverty, since dark, crowded quarters and inadequate diets usually fall to the lot of the poor. But in India the opposite is true—the better class Mohammedan women, and in most places the highest caste Hindu women, whose part-time husbands may be wealthy enough to clothe them in pearls and feed them on hummingbirds, live their entire adult lives in purdah, secluded in poorly lighted rooms furnished with jewel-studded walls and alabaster baths, but with few or no windows. Their only outings are on the occa-

sion of family marriages or deaths, or of religious ceremonies, when they go forth draped somewhat more effectively than a Ku Klux Klansman at a lynching. Among these women, fed on the richest food money can buy, osteomalacia is more common than it is in the slums of New York, and many of their babies have rickets, while among the teeming millions of India's lower castes who are abundantly exposed to the sun, rickets and osteomalacia are practically never seen. In parts of China, also, osteomalacia is prevalent among a certain class of women—not the poor ones, who have to work in the fields, or the rich ones who can add meat and fat to their diet of millet gruel, but those who are too proud to work but too poor to eat well.

The speed with which improvement in rickets and osteomalacia can be brought about is amazing. Deposit of lime and resumption of normal bone growth may begin within twenty-four hours after cod-liver oil is administered, but in severe cases it may take several months of treatment to get complete cures. Three teaspoonfuls a day is usually considered a good curative dose, but rapid cures of bad cases may require considerably more. Although excessive doses of vitamin D have been found to cause premature calcification of bones, and deposits of calcium where none should be, and also to produce other toxic symptoms, the doses necessary to produce these effects are thousands of times larger than the ordinary doses, so danger of too much vitamin D is too remote to cause any worry to a mother or physician.

Occasional individuals require much larger doses of vitamin D to cure or prevent rickets than the average. Premature babies sometimes need 10,000 to 20,000 units a day, and there is one case of a boy of sixteen years, whose rickets had persisted from infancy in spite of orthodox methods of

treatment, to whom 1,000,000 to 1,500,000 units a day had to be given before healing began, and when recovered he had to get 150,000 a day to keep him normal. Before modern methods of concentrating vitamin D were invented it would have been impossible to cure him, for it would have taken ten to fifteen quarts of cod-liver oil to supply the necessary number of daily units. The unconcentrated liver oil of the blue-fin tuna is 400 times as potent as cod-liver oil, and some vitamin D concentrates are several thousand times as potent. Nowadays the oils extracted from the livers of various kinds of fish are mixed together in such a way as to provide 100 times as much of both vitamin A and vitamin D as standard cod-liver oil.

Large doses of vitamin D have been found by some scientists to be effective, sometimes at least, in the treatment of a number of conditions in which its function is more obscure than in rickets. Among these are celiac disease, arthritis, hay fever, psoriasis (a common skin disorder in the North), milk fever, and even near-sightedness. It is also claimed to increase resistance to infantile paralysis, and to hasten the healing of wounds when locally applied.

VITAMIN E, THE STORK VITAMIN

During the post-war days when the goodness of a diet had been found to involve more than calories and proteins, and the new alphabet of vitamins was becoming a prominent feature of nutritional studies, two scientists at the University of California made an interesting observation. Their female rats fed on a diet containing all the vitamins a rat was known to have any use for were found to be perfectly normal in every respect except their inability to produce families. They had normal sex cycles, normal conceptions,

and began their pregnancies in a normal manner, but they never became more than expectant mothers. Their young died in the uterus after the middle of the period of pregnancy (which is twenty-one days) and were re-absorbed. Suspecting that this might be a rat's reaction to lack of vitamin C, which rats were supposed not to need in their food, these scientists added orange juice to the diet of one group of rats, and lettuce to that of another. Only about one in each five or six of the orange-fed rats succeeded in producing a litter, whereas the lettuce-fed rats all had blessed events.

This was the beginning of knowledge of a special substance in the diet without which normal reproduction fails, at least in rats. Subsequently it was found that this substance, which was christened vitamin E in 1923, is necessary for rapidly multiplying cells. In the female, which produces only one egg to millions of sperms in the male, the lack of the vitamin produces no effect in the ovary, but does affect the rapidly multiplying cells of the fetus and also the placenta, through which the fetus is nourished. In males, on the other hand, the cells lining the tubules of the testes, from which millions of sperms are constantly being formed in adult life, are among the most rapidly multiplying cells in the body. A male rat deprived of vitamin E at first has normal sex power and apparently normal sperms, but the sperms fail to fertilize the eggs. Subsequently no sperms are produced, then there is loss of sexual vigor, and finally loss even of sexual interest. Another site of rapid cell multiplication is in the brain of rats shortly after birth. Baby rats born of mothers deficient in vitamin E are likely to develop paralysis when about three weeks old.

Other vitamins, when fed to animals which have been deprived of them, bring about rapid or even spectacular im-

provement, but in rats damage done by lack of vitamin E is usually there to stay. Feeding of vitamin E begun after five days of pregnancy is too late to save a litter. Males sterile from lack of the substance sometimes recover but it takes nearly a year of treatment, which brings a rat close to middle age. A very small amount of the vitamin enables female rats to become mothers if given in early maturity, but as the rats grow older they require more and more. Rats deprived of vitamin E until over a year old are never able to reproduce however much of the fertility vitamin they are then given.

That vitamin E may have other functions is indicated by the fact that rabbits and guinea pigs experience a wasting away of their muscles when deprived of it, and can be cured by its administration.

As has been observed before, what is good for a rat is in most cases good for human beings also. There is strong evidence that vitamin E is necessary to mankind as well as to rats for successful reproduction, and that occasionally human beings may be inadequately supplied with it in their normal diets. Largely on the basis of its effects in rats it has been postulated that inadequate vitamin E in human beings might lead not only to a high abortion rate in women but to a low rate of fertility in men.

Many cases of sterility are correlated either with too few sperms, or inactive or lifeless ones, or a high percentage of misshapen ones. Sometimes these defects respond to continued treatment with pituitary extract, but often they do not, and in many of these cases there is no good explanation for the condition. In view of the effects of insufficient vitamin E on male rats, it is possible that the human males who are unable to contribute to posterity on account of the production of too few, too sluggish, or imperfectly formed

sperms may be suffering from too little of vitamin E, or inability to assimilate it.

There is growing evidence that during pregnancy a deficiency of vitamin E is much commoner than had been supposed. Drastic changes in metabolism occur during pregnancy; more vitamins than usual are needed, and relative deficiency in one or all may be the cause of many of the discomforts and accidents that go with child-bearing. A few years ago a Danish doctor treated twenty women, who were given to habitual abortions, with wheat germ oil, the richest known source of vitamin E, and seventeen of them gave birth to normal nine-month babies. A doctor in England gave three small capsules of extract of wheat germ oil daily to a series of expectant mothers for an average of five months before their babies were due, and got only one abortion in a group of twenty-three mothers who previously had a record of only eleven living children out of seventy-three pregnancies, five of which died immediately after birth. Two doctors at the University of Western Ontario gave 2 or 3 drams a day of wheat germ oil to forty-six women who had a history of one or more previous abortions, and got thirty-four normal deliveries, and of nineteen other cases of threatened abortion, thirteen produced normal babies.

Another man at the same Canadian school has found that vitamin E is also an excellent treatment for premature separation of the placenta from the uterus. When extensive, this causes severe shock, often with profuse bleeding, and leads to the death of the fetus and often of the mother as well. More commonly the separation is only partial, causing mild bleeding, pains, and tenderness in the uterus, severe aches in the lower back, and often abortions. In these cases consistently good results were reported from treatment with wheat germ oil if begun early enough. A

simple chemical test of the serum by which an inadequate supply of vitamin E can be detected has also been reported, making it possible to diagnose vitamin E deficiency without guessing at it. Apparently vitamin E has a neutralizing effect on the ovarian hormone (oestrin); when this hormone is too abundant it interferes with the burrowing into the uterine wall of the placental villi which make for a firm union. The blood of a high percentage of women with spontaneous abortions is said to show evidence of vitamin E deficiency by the serum test, but a normal condition is restored by a single large dose (6 to 12 drams) of wheat germ oil, or repeated smaller doses of 2 to 3 drams daily for a few days. Possibly lack of vitamin E will be found to be the underlying cause of other obscure reproductive ailments.

Vitamin E, like A and D, is soluble in fats. It has recently been obtained as a pure chemical known as alpha-tocopherol. It is not injured by cooking, drying, or ordinary exposure to air, but is quickly destroyed by rancidity of the fats in which it is dissolved, and also by some iron salts. It is very widely distributed in Nature, having been found in green leaves and other vegetable foods, as well as in the meat, fat, eggs, and milk of animals fed on E-containing foods, but it is particularly abundant in the germinal parts of seeds. The most abundant source so far known is wheat germ or rice germ oil. Most people certainly obtain plenty of vitamin E in their usual diets, but there is evidence that in rats some individuals, even among litter mates, assimilate and store vitamin E far less readily than others, and this may also be true of human beings. Probably an unusually large amount is required during pregnancy to react with the large quantity of oestrin formed or stored in the placenta, and it is only then that the effect of diets low in this vitamin would become apparent. It is doubtful whether special food preparations

rich in vitamin E should be advertised as general stork lures, but the use of such foods or of the extracted oil of seed germs is certainly desirable in cases with histories or premonitions of abortion, and might well be tried on both partners, but particularly the man, in the six or eight cases of sterility out of every hundred that cannot be accounted for on the basis of diseased or abnormal anatomical conditions.

VITAMIN K, THE BLOOD-CLOTTING VITAMIN

A few years ago it was discovered that chicks fed on certain experimental diets which contained the entire quota of vitamins and factors known up to date developed a tendency to bleed—from cuts, broken pin feathers, or apparently without provocation—and just kept on bleeding. Examination of the blood showed that it lacked prothrombin, an essential ingredient which enables blood to clot on exposure to air. The chicks could be saved from bleeding to death by addition of only 1 per cent of dry alfalfa to their food, whereas 2 per cent brought them back to normal. It was also observed that their feathers grew better when the alfalfa was added. Further investigation showed that the new food factor, christened vitamin K, is a fat-soluble substance found in unusual abundance in alfalfa, but also present in various other vegetables, such as cabbage, spinach, and tomatoes, in the liver fat of hogs, and in fish meal.

Within the present year the chemical nature of vitamin K has been determined and a pure synthetic form of it—a naphthoquinone—has been manufactured. This is so potent that one gram of it is equivalent to the extract from 500 lbs. of alfalfa.

Although the bleeding disease has not been induced in animals other than chicks by giving a diet deprived of vita-

min K, there is good evidence that this vitamin will cure unrestrained bleeding wherever prothrombin is deficient. In cattle and rabbits, for instance, a loss of prothrombin results from eating improperly cured sweet clover. This can be prevented by adding 5 per cent dry alfalfa to the feed.

In human beings surgeons have long been worried about what to do in cases of "obstructive jaundice." This is a condition in which the bile ducts get clogged up so the bile is unable to reach the intestine and is deposited elsewhere in the body, causing the sufferer to acquire a saffron-tinted skin and eyes. The obvious procedure would seem to be an operation to open a passage through the stopped-up tubes, but this is often impossible because in obstructive jaundice the blood frequently fails to clot, in which case the patient would promptly bleed to death. Some doctors at the Mayo Clinic, pondering over the effect of alfalfa on bleeding chicks and rabbits, and believing the bleeding of their jaundiced patients might be the result of inability to absorb fat-soluble vitamin K in the absence of bile, began feeding their cases on alfalfa meal, but since the patients did not take kindly to this, they later used fish meal instead, along with some bile to facilitate absorption, and got very good results.

Another very promising use for vitamin K is in the prevention and cure of bleeding in new-born babies. During the first few days of life the blood-clotting time of babies is likely to fluctuate so a graph of it looks like a stock market chart during a series of war scares, but by about the fifth day it steadies down and remains at a reasonably low level. Meanwhile even a very small bleeding point may lead to great loss of blood. In such cases a single dose of vitamin K concentrate may, within one and a half to two hours, cut the blood-clotting time in half. Bleeding inside the brain case is responsible for from 25 to 40 per cent of deaths of new-born

babies; few maternity hospitals escape without at least one case in 100 to 150 births, and many of the babies so unfortunate as not to die become physical and mental cripples. Some doctors at the University of Virginia think that many of these cases, caused by slow, oozing hemorrhages from small bleeding points, could be prevented by giving vitamin K immediately after birth, or perhaps by giving it to the mother shortly before delivery. It might also be of benefit to mothers who are slow to stop bleeding after the birth of a baby. With the recent development of a pure synthetic form of vitamin K which can be intravenously injected, it is probable that a much wider use will be made of it.

A fatty substance has recently been obtained from animal livers which has a remarkable effect in checking excessive menstrual bleeding; the relation of this "anti-menorrhagic factor" to vitamin K is still somewhat uncertain.

In conclusion it should also be mentioned that injection of small amounts of oxalic acid, a well-known ink remover, also has striking effects in causing blood to coagulate. This might well be included in a "believe it or not" column, since salts of oxalic acid in larger amount have long been used to *prevent* coagulation of blood which has been drawn for experimental purposes.

THE USE OF SUPPLEMENTARY VITAMINS

It is obvious from what has been said about the important functions of the various vitamins, and about the extent to which they may be missing in modern American diets, that the use of supplementary vitamins is often desirable, or even necessary, to insure maximum health.

Modern methods of concentrating vitamins or of synthetically manufacturing them have made it possible to sup-

ply them in purified form at no appreciably greater cost, if not actually cheaper, than foods naturally containing them. The use of such purified vitamins would in the past have been undesirable because we were not certain just what vitamins a human being really needed. If we had attempted to substitute thiamin (pure vitamin B_1) for the vitamin B complex found in natural foods, we would have deprived ourselves of such other necessary vitamins as nicotinic acid, riboflavine, and possibly others. It is not certain that we know all the vitamins we need even yet, and it is possible that the use of entirely vitaminless food with purified vitamins added would bring to light hitherto unsuspected food requirements, as it has done in the case of experimental animals.

However, we could probably get along excellently with any ordinary foods for which we might take a fancy, as long as they supplied us with adequate calories and proteins, if we supplemented them with known vitamins and minerals in a concentrated or purified state. With the use of such preparations we could give our appetites much freer rein, and we could cease to worry very much about the likes and dislikes of little Willie.

Few people would need or desire to get all or even most of their vitamins or minerals in pills, but it would constitute an excellent "diet insurance" for people who are reducing; for people with finicky appetites, diabetes, irritable digestive tracts, or other conditions interfering with normal food consumption; and for people suffering from food shortages on expeditions or in times of war or famine. It will probably not be long until we are adding vitamins and minerals to staple foods as we already add iodine to salt. We already look favorably on cod-liver oil and orange juice as adjuncts to a baby's diet, purely for their vitamin content. We may soon be getting thiamin in our sugar, nicotinic acid and

riboflavine in our salt, pure distilled vitamins A and D in our milk or butter, vitamin C in our citrus or tomato juice. As Dr. Milo Hastings remarked in a recent article, "the fact that man frequently errs by flouting nature does not prove that he cannot beat nature at her own game by stealing her thunder and making it louder. Much of human progress has been achieved in that fashion."

When symptoms of vitamin deficiencies have actually made themselves apparent, it is nearly always necessary to turn to concentrated or pure vitamins for treatment. Such symptoms result from long-continued lack of vitamin-bearing foods, improper preparation of them, or failure to absorb them in a normal manner. To correct such conditions requires drastic changes in dietary habits, which are often difficult because man is a creature of habit and has a tendency to develop strong likes and dislikes with respect to his victuals. Moreover, it may be necessary to give a great excess of one or several vitamins until a normal condition is restored. It would often be physically impossible for a person to eat enough food to obtain the amounts of vitamins needed to bring about a reasonably rapid cure of such conditions as scurvy, pellagra, beri-beri, and rickets.

Asa C. Chandler.

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